```
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):s chlorpropamide
       2383804 S
           999 CHLORPROPAMIDE
             0 S CHLORPROPAMIDE
L3
                  (S(W)CHLORPROPAMIDE)
=> s chlorpropamide and vanadium
           999 CHLORPROPAMIDE
         40027 VANADIUM
L4
           151 CHLORPROPAMIDE AND VANADIUM
=> s 14 and vanadyl sulfate
          3544 VANADYL
        231630 SULFATE
           682 VANADYL SULFATE
                 (VANADYL (W) SULFATE)
L5
           112 L4 AND VANADYL SULFATE
=> s 16 and pd< 1998
L6 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).
=> s 15 and pd < 1998
       2268293 PD< 1998
                 (PD<19980000)
1.6
             0 L5 AND PD< 1998
=> d his
     (FILE 'HOME' ENTERED AT 13:47:58 ON 21 MAY 2003)
     FILE 'USPATFULL' ENTERED AT 13:48:11 ON 21 MAY 2003
L1
            113 S DIABETES AND VANADYL SULFATE AND CHLORPROPAMIDE
L2
              0 S L1 AND PD<1998
L3
              0 S S CHLORPROPAMIDE
L4
            151 S CHLORPROPAMIDE AND VANADIUM
L_5
            112 S L4 AND VANADYL SULFATE
L6
              0 S L5 AND PD< 1998
=> s 14 and pd<1998
       2268293 PD<1998
                 (PD<19980000)
L7
             3 L4 AND PD<1998
=> d 17 1=3 kwic, bib
'1=3' IS NOT VALID HERE
Your input could not be processed as entered. For more help, please
enter "HELP DISPLAY UNIT" at an arrow prompt (=>).
=> d 17 1-3 kwic, bib
L7
     ANSWER 1 OF 3 USPATFULL
PI.
       US 6297269
                          В1
                               20011002
       WO 9639385 19961212
SUMM
       . . . and its subsequent widespread use in the treatment of diabetes,
       and the later discovery of and use of sulfonylureas (e.g.
       Chlorpropamide.TM. (Pfizer), Tolbutamide.TM. (Upjohn),
       Acetohexamide.TM. (E. I. Lilly), Tolazamide.TM. (Upjohn)) and biguanides
       (e.g. Phenformin.TM. (Ciba Geigy), Metformin.TM. (G. D. Searle)) as. .
```

```
. agents such as insulin and insulin analogs (e.g. LysPro
SUMM
       insulin); GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)-NH.sub.2;
      Sulfonylureas and Analogs: chlorpropamide, glibenclamide,
       tolbutamide, tolazamide, acetohexamide, glypizide.RTM., glimepiride,
       repaglinide, meglitinide; Biguanides: metformin, phenformin, buformin;
       .alpha.2-Antagonists and Imidazolines: midaglizole, isaglidole,
       deriglidole, idazoxan, efaroxan,. . . 35135, BRL 37344, Ro 16-8714,
       ICI D7114, CL 316,243; Phosphodiesterase Inhibitors: L-386,398;
       Lipid-lowering Agents: benfluorex; Antiobesity Agents: fenfluramine;
       Vanadate and vanadium complexes (e.g. naglivan.RTM.) and
       peroxovanadium complexes; Amylin Antagonists; Glucagon Antagonists;
       Gluconeogenesis Inhibitors; Somatostatin Analogs; Antilipolytic Agents:
       nicotinic acid, acipimox, WAG.
CLM
       What is claimed is:
          and Imidazolines; insulin secretagogues; Glitazones; Fatty Acid
       Oxidation inhibitors; .alpha.-Glucosidase inhibitors; .beta.-Agonists;
       Phosphodiesterase Inhibitors; Lipid-lowering Agents; Antiobesity Agents;
       Vanadate and vanadium complexes and peroxovanadium complexes;
       Amylin Antagonists; Glucagon Antagonists; Gluconeogenesis Inhibitors;
       Somatostatin Analogs; Antilipolytic Agents; and c) optionally a
       pharmaceutically acceptable.
       2001:168152 USPATFULL|
AN
       Substituted n-(indole-2-carbonyl-) amides and derivatives as glycogen
TΙ
       phosphorylase inhibitors|
       Hulin, Bernard, Essex, CT, United States
IN ·
       Hoover, Dennis J., Stonington, CT, United States
       Treadway, Judith L., Gales Ferry, CT, United States
       Martin, William H., Essex, CT, United States
Pfizer Inc., New York, NY, United States (U.S. corporation).
PA
       US 6297269
                          В1
                               20011002
PΙ
                                                                      <--
       WO 9639385 19961212
       US 1997-952668
                               19971202 (8)
ΑI
       WO 1995-IB443
                               19950606
                               19971202
                                         PCT 371 date
                                19971202 PCT 102(e) date
DΤ
       Utility|
FS
       GRANTED |
       Primary Examiner: Ramsuer, Robert W.; Assistant Examiner: Keating,
EXNAM
LREP
       Richardson, Peter C., Benson, Gregg C., Olson, A. Dean
CLMN
       Number of Claims: 77|
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 43181
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L7
     ANSWER 2 OF 3 USPATFULL
       US 6107329
                                20000822
PΙ
       WO 9639384 19961212
               and its subsequent widespread use in the treatment of diabetes,
SUMM
       and the later discovery of and use of sulfonylureas (e.g.
       Chlorpropamide.TM. (Pfizer), Tolbutamide.TM. (Upjohn),
       Acetohexamide.TM. (E. I. Lilly), Tolazamide.TM. (Upjohn)) and biguanides
       (e.g. Phenformin.TM. (Ciba Geigy), Metformin.TM. (G. D. Searle)) as.
SUMM
                agents such as insulin and insulin analogs (e.g. LysPro
       insulin); GLP-1 (7-37) (insulinotropin) and GLP-1 (7-36)-NH.sub.2;
       Sulfonylureas and Analogs: chlorpropamide, glibenclamide,
       tolbutamide, tolazamide, acetohexamide, glypizide.RTM., glimepiride,
       repaglinide, meglitinide; Biguanides: metformin, phenformin, buformin;
       .alpha.2-Antagonists and Imidazolines: midaglizole, isaglidole,
       deriglidole, idazoxan, efaroxan, . . 35135, BRL 37344, Ro 16-8714,
```

```
ICI D7114, CL 316,243; Phosphodiesterase Inhibitors: L-386,398;
       Lipid-lowering Agents: benfluorex; Antiobesity Agents: fenfluramine;
       Vanadate and vanadium complexes (e.g. naglivan.RTM.) and
       peroxovanadium complexes; Amylin Antagonists; Glucagon Antagonists;
       Gluconeogenesis Inhibitors; Somatostatin Analogs; Antilipolytic Agents:
       nicotinic acid, acipimox, WAG.
AN
       2000:109834 USPATFULL
       Substituted n-(indole-2-carbonyl)-glycinamides and derivatives as
ΤI
       glycogen phosphorylase inhibitors
       Hoover, Dennis J., Stonington, CT, United States
IN
       Hulin, Bernard, Essex, CT, United States
       Martin, William H., Essex, CT, United States
       Phillips, Douglas, Gales Ferry, CT, United States
       Treadway, Judith L., Gales Ferry, CT, United States
       Pfizer, Inc., New York, NY, United States (U.S. corporation)
PA
                               20000822
PΙ
       US 6107329
       WO 9639384 19961212
       US 1997-952669
                               19971202 (8)
ΑI
       WO 1995-IB442
                               19950606
                                         PCT 371 date
                               19971202
                               19971202 PCT 102(e) date
DT
       Utility
       Granted
FS
EXNAM
       Primary Examiner: Riley, Jezia
       Richardson, Peter C., Benson, Gregg C., Olson, A. Dean
LREP
       Number of Claims: 44
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 5662
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
T.7
     ANSWER 3 OF 3 USPATFULL
                               19900925
PΙ
       US 4959212
             . daily dosage of either 1.25-20 mg. of glyburide--1-[(p-(5- ^{\circ}
SUMM
       chloro-o-anisamido) ethyl) phenyl)-sulfonyl] 3-cyclohexylurea--sold
       under the registered trademark Micronase.RTM. or 125-750 mg. of
       chlorpropamide--1-((p-chlorophenyl)-sulfonyl) 3-propylurea--sold
       under the trademark Diabinese.RTM..
DETD
                The disodium salt exhibits limited stability in water and is
       not stable in the presence of some impurities, such as vanadium
       . These instability problems limit its use in the inventive
       compositions.
               glucose concentration used as a daily dose, the antidiabetic
DETD
       drug generally will be selected from the group consisting of glyburide,
       chlorpropamide, tolbutamide and tolazamide. Generally, the daily
       dosages of such antidiabetic drugs will be in the following ranges: 1.25
       to 20 mg. of glyburide (Micronase.RTM.; 125 to 750 mg. of
       chlorpropamide (Diabinese.RTM.); 250 to 1250 mg of tolbutamide
       (Orinase.RTM.); and 250 to 1250 mg. of tolazamide (Tolinase.RTM.). The
       described drug dosages.
       Example 3 is repeated with the exception that 750 mg./day of
DETD
       chlorpropamide in the form of Diabinase.RTM. tablets is used as
       the antidiabetic drug. The carbohydrate ingestion value is 115-125
       mg./day for.
       What is claimed is:
CLM
          is selected from the group consisting of 1.25 mg. to 20 mg. of
       glyburide, 125 mg. to 750 mg. of chlorpropamide, 250 mg. to
       1250 mg. of tolbutamide and 250 mg. to 1250 mg. of tolazamide, said
       concentrations being the total.
          is selected from the group consisting of 1.25 mg. to 20 mg. of
       glyburide, 125 mg. to 750 mg. of chlorpropamide, 250 mg. to
       1250 mg. of tolbutamide and 250 mg. to 1250 mg. of tolazamide is
```

```
administered, said drug concentration. . .
       90:74947 USPATFULL|
AN
       Oxidizing-energizing composition and method for the treatment of
ΤI
       diabetes|
       Stancesco, Alexandra, 1184 Main St., Apt. 75, River Edge, NJ, United
ΙN
       States 07661
       Spiliadis, Apostol, 5-D Patton Dr., Bloomfield, NJ, United States 07003
       Dumas, Theodore, 977 Waterloo Street, Ontario, London, Canada N 6 A 2 x
ΡI
       US 4959212
                               19900925
ΑI
       US 1988-209877
                               19880622 (7)
DT
       Utility|
FS
       Granted|
EXNAM
       Primary Examiner: Stone, Jacqueline; Assistant Examiner: Witz, Jean C.|
LREP
       Miller, Richard N. |
CLMN
       Number of Claims: 21|
       Exemplary Claim: 1|
ECL
DRWN
       No Drawings
LN.CNT 935|
```

=>

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
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                 Web Page URLs for STN Seminar Schedule - N. America
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         Jun 03
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                 PHARMAMarketLetter(PHARMAML) - new on STN
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         Aug 08
NEWS
         Aug 19
                 Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS
     6
         Aug 26
                 Sequence searching in REGISTRY enhanced
NEWS 7
         Sep 03
                 JAPIO has been reloaded and enhanced
         Sep 16
                 Experimental properties added to the REGISTRY file
NEWS
NEWS 9
         Sep 16
                 CA Section Thesaurus available in CAPLUS and CA
        Oct 01
NEWS 10
                 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11
         Oct 24
                 BEILSTEIN adds new search fields
NEWS 12
         Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13
        Nov 18
                 DKILIT has been renamed APOLLIT
NEWS 14
         Nov 25
                 More calculated properties added to REGISTRY
NEWS 15
         Dec 04
                 CSA files on STN
         Dec 17
NEWS 16
                 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17
         Dec 17
                 TOXCENTER enhanced with additional content
NEWS 18
         Dec 17
                 Adis Clinical Trials Insight now available on STN
NEWS 19
         Jan 29
                 Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
NEWS 20
         Feb 13
                 CANCERLIT is no longer being updated
NEWS 21
        Feb 24
                METADEX enhancements
NEWS 22
        Feb 24
                PCTGEN now available on STN
NEWS 23 Feb 24 TEMA now available on STN
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25
        Feb 26 PCTFULL now contains images
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27
        Mar 20 EVENTLINE will be removed from STN
NEWS 28
        Mar 24 PATDPAFULL now available on STN
NEWS 29
        Mar 24
                Additional information for trade-named substances without
                 structures available in REGISTRY
NEWS 30
        Apr 11
                 Display formats in DGENE enhanced
NEWS 31
        Apr 14
                 MEDLINE Reload
NEWS 32
        Apr 17
                 Polymer searching in REGISTRY enhanced
         Apr 21
NEWS 33
                 Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34
        Apr 21
                 New current-awareness alert (SDI) frequency in
                 WPIDS/WPINDEX/WPIX
NEWS 35
        Apr 28
                 RDISCLOSURE now available on STN
        May 05
                 Pharmacokinetic information and systematic chemical names
NEWS 36
                 added to PHAR
NEWS 37
        May 15
                 MEDLINE file segment of TOXCENTER reloaded
NEWS 38
        May 15
                 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39
        May 16
                 CHEMREACT will be removed from STN
NEWS 40
        May 19
                 Simultaneous left and right truncation added to WSCA
NEWS 41
        May 19
                 RAPRA enhanced with new search field, simultaneous left and
                 right truncation
```

MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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SINCE FILE TOTAL
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 20 May 2003 (20030520/PD)
FILE LAST UPDATED: 20 May 2003 (20030520/ED)
HIGHEST GRANTED PATENT NUMBER: US6567988
HIGHEST APPLICATION PUBLICATION NUMBER: US2003093849
CA INDEXING IS CURRENT THROUGH 20 May 2003 (20030520/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 20 May 2003 (20030520/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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999 CHLORPROPAMIDE
L1
=> s 11 and pd<1999
       2435280 PD<1999
                 (PD<19990000)
           459 L1 AND PD<1999
L2
=> s l1 and pd<1998
       2268293 PD<1998
                 (PD<19980000)
L3
           421 L1 AND PD<1998
=> s l1 and pd<1997
       2136955 PD<1997
                 (PD<19970000)
L4
           386 L1 AND PD<1997
=> s 11 and pd<1996
       2009370 PD<1996
                 (PD<19960000)
           359 L1 AND PD<1996
=> s 15 and vanadyl sulfate
          3544 VANADYL
        231630 SULFATE
           682 VANADYL SULFATE
                 (VANADYL (W) SULFATE)
             0 L5 AND VANADYL SULFATE
L6
=> s 14 and vanadyl sulfate
          3544 VANADYL
        231630 SULFATE
           682 VANADYL SULFATE
                 (VANADYL (W) SULFATE)
L7 :
             0 L4 AND VANADYL SULFATE
=> s 13 and vanadyl sulfate
          3544 VANADYL
        231630 SULFATE
           682 VANADYL SULFATE
                  (VANADYL(W)SULFATE)
L8
             0 L3 AND VANADYL SULFATE
=> d his
     (FILE 'HOME' ENTERED AT 14:37:46 ON 21 MAY 2003)
     FILE 'USPATFULL' ENTERED AT 14:38:21 ON 21 MAY 2003
L1
            999 S CHLORPROPAMIDE
L2
            459 S L1 AND PD<1999
            421 S L1 AND PD<1998
L3
            386 S L1 AND PD<1997
L4
L5
            359 S L1 AND PD<1996
L6
              0 S L5 AND VANADYL SULFATE
L7
              0 S L4 AND VANADYL SULFATE
              0 S L3 AND VANADYL SULFATE
T8
=> s 12 and vanadyl sulfate
          3544 VANADYL
        231630 SULFATE
           682 VANADYL SULFATE
```

(VANADYL (W) SULFATE)

=> d 19

```
ANSWER 1 OF 1
L9
                   USPATFULL
       1998:153865 USPATFULL
AN
       Composition and method for reducing blood sugar levels in diabetic
TΙ
       Al-Dahir, Holly Christine, 4521 Conlin St., Metairie, LA, United States
ΙN
       70006
PΙ
       US 5846544
                               19981208
ΑI
       US 1997-891590
                               19970711 (8)
DT
       Utility
FS
       Granted
LN.CNT 245
INCL
       INCLM: 424/195.100
       INCLS: 514/783.000; 514/866.000; 514/884.000
NCL
       NCLM: 424/732.000
       NCLS: 514/783.000; 514/866.000; 514/884.000
IC
       ICM: A61K035-78
EXF
       424/195.1; 514/783; 514/866; 514/884
=> d his
     (FILE 'HOME' ENTERED AT 14:37:46 ON 21 MAY 2003)
     FILE 'USPATFULL' ENTERED AT 14:38:21 ON 21 MAY 2003
            999 S CHLORPROPAMIDE
L1
L2
            459 S L1 AND PD<1999
L3
            421 S L1 AND PD<1998
L4
            386 S L1 AND PD<1997
L5
            359 S L1 AND PD<1996
              0 S L5 AND VANADYL SULFATE
L6
              0 S L4 AND VANADYL SULFATE
L7
              0 S L3 AND VANADYL SULFATE
L8
L9
              1 S L2 AND VANADYL SULFATE
=> d 19 kwic
L9
     ANSWER 1 OF 1 USPATFULL
       US 5846544
PΙ
                               19981208
DETD
          . . 5'6" tall had Type II non-insulin dependent diabetes mellitus
       for four years, being maintained on a sulfonylulurea hypoglycemic agent,
       specifically chlorpropamide, as well as being maintained on a
       blood pressure medication and a weight controlled medication, and not on
       a diabetic.
DETD
       It is noted that, beginning one month before initial dosage of the
       herbs, subject took vanadyl sulfate (5,000 mcg)
       chromium picolinate (250 mcg), and a multi-vitamin capsule once daily
       with a meal, with no effect on blood sugar level. Vanadyl
       sulfate and chromium picolinate are know hyproglycemic agents.
       When subject's blood sugar level was reduced to approximately 200 mg/dl,
       subject began.
       Subject is on vitamin and mineral supplements, including vanadyl
DETD
       sulfate and chromium picolinate and gymnema sylvestre, which are
       known hypoglycemic agents.
DETD
          . . reducers such as penicillin and its derivatives such as,
       amoxycillin, as well as mineral hypoglycemic agents as chromium
       picolinate and vanadyl sulfate, (iv) insulin
```

dependent diabetes mellitus subjects will experience hyperglycemia

```
=> d 15 359, 1
L5
     ANSWER 359 OF 359 USPATFULL
AN
       72:32607 USPATFULL
TI
       EXO-DIBICYCLOALKANE CARBOXAMIDES
       Rynbrandt, Ronald H., Portage, MI, United States
IN.
       The Upjohn Company, Kalamazoo, MI, United States
PA
PΙ
       US 3673197
                                19720627
       US 1971-106602
                                19710114 (5)
ΑI
DT
       Utility
FS
       Granted
LN.CNT 506
INCL
       INCLM: 260/295.000AM
       INCLS: 260/557.000B; 260/295.000D; 260/295.000K; 424/320.000;
              424/263.000
NCL
       NCLM:
              546/309.000
              514/866.000; 564/152.000; 564/155.000; 564/158.000
       NCLS:
TC
       [1]
       ICM: C07D031-44
       ICS: C07C103-19
       260/557B; 260/295AM; 260/295R; 260/295D
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 1 OF 359 USPATFULL
L5
ΑN
       1999:140916 USPATFULL
       Controlled release device and method
TI
       Cardamone, Michael, Thomastown, Australia
IN
       Bentley, Herbert William, Sylvania, Australia
       Controlled Release Technologies Pty Ltd, Victoria, Australia (non-U.S.
PA
       corporation)
                                19991109
ΡI
       US 5980508
       WO 9535131 19951228
                                                                      <--
       US 1997-750894
                                19970430 (8)
ΑI
       WO 1995-AU366
                                19950622
                                19970430
                                          PCT 371 date
                                          PCT 102(e) date
                                19970430
PRAI
       AU 1994-6413
                            19940622
       AU 1995-1866
                            19950321
DT
       Utility
FS
       Granted
LN.CNT 1424
INCL
       INCLM: 604/890.100
NCL
       NCLM:
              604/890.100
IC
       [6]
       ICM: A61K009-22
EXF
       604/892.1; 604/890.1; 604/891.1; 424/449; 424/473
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
=> d 15 1,359 kwic
L5
     ANSWER 1 OF 359
                      USPATFULL
PΙ
       US 5980508
                                19991109
       WO 9535131 19951228
                tetracyclin compounds, vasodilators, acetaminiophen,
SUMM
       acetazolamide, acetophenetidin, achromycine hydrochloride,
       bendofluazide, benzthiozide, betamethasone, calcium and salts, thereof
       including, leucovorin calcium, carbamazepine, clindamycin,
       chlorpropamide, chlorothalidone, chlorothiazide, clofibrate,
```

cortisone acetate, cyclopenthiazide, dexamethazone, dextroamphetamine sulphate, diclofenac sodium, digoxin, dimethindene and salts thereof, diprophylline, disopyramide and salts. . .

L5 ANSWER 359 OF 359 USPATFULL

PI US 3673197

19720627

DETD

. . . active ingredients, the present compositions can also include, as supplementary active ingredients, other blood sugar lowering compounds, such as tolbutamide, **chlorpropamide**, and phenformin. Such supplementary active ingredients can be included in these compositions in amounts approximately equal to or less than. .

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right truncation

CHEMREACT will be removed from STN

MEDLINE file segment of TOXCENTER reloaded

Supporter information for ENCOMPPAT and ENCOMPLIT updated

RAPRA enhanced with new search field, simultaneous left and

Simultaneous left and right truncation added to WSCA

NEWS 37

NEWS 38

NEWS 39

NEWS 40

NEWS 41

May 15

May 15

May 16

May 19

May 19

MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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FILE 'USPATFULL' ENTERED AT 12:45:11 ON 21 MAY 2003 CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 20 May 2003 (20030520/PD)
FILE LAST UPDATED: 20 May 2003 (20030520/ED)
HIGHEST GRANTED PATENT NUMBER: US6567988
HIGHEST APPLICATION PUBLICATION NUMBER: US2003093849
CA INDEXING IS CURRENT THROUGH 20 May 2003 (20030520/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 20 May 2003 (20030520/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

	HCDAMO is now somilable. HCDAMENTI sometime full book of the	<<<
>>>	USPAT2 is now available. USPATFULL contains full text of the	
>>>	original, i.e., the earliest published granted patents or	<<<
>>>	applications. USPAT2 contains full text of the latest US	<<<
>>>	publications, starting in 2001, for the inventions covered in	<<<
>>>	USPATFULL. A USPATFULL record contains not only the original	<<<
>>>	published document but also a list of any subsequent	<<<
>>>	publications. The publication number, patent kind code, and	<<<
>>>	publication date for all the US publications for an invention	<<<
>>>	are displayed in the PI (Patent Information) field of USPATFULL	<<<
>>>	records and may be searched in standard search fields, e.g., /PN,	<<<
>>>	/PK, etc.	<<<
>>>	USPATFULL and USPAT2 can be accessed and searched together	<<<
>>>	through the new cluster USPATALL. Type FILE USPATALL to	<<<
>>>	enter this cluster.	<<<
>>>		<<<
>>>	Use USPATALL when searching terms such as patent assignees,	<<<
>>>	classifications, or claims, that may potentially change from	<<<

US 2002-93476

US 2001-278270P

US 2001-278271P US 2001-278296P

ΑI

PRAI

A1

20020307 (10)

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20010322 (60)

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     ANSWER 3 OF 52, USPATFULL
L2
AN
       2003:112605 USPATFULL
       Formulations for the prevention and treatment of insulin resistance and
TΙ
       type 2 diabetes mellitus
       Richardson, Kenneth T., Anchorage, AK, UNITED STATES
IN
       Pearson, Don C., Lakewood, WA, UNITED STATES
       ChronoRX LLC, Anchorage, AK (U.S. corporation)
PA
                                20030424
PI
       US 2003077335
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       US 2001-33730
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ΑI
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L2
     ANSWER 4 OF 52 USPATFULL
AN
       2003:100081 USPATFULL
       Inhibition by 3-deoxyflavonoids of T-lymphocyte activation and therapies
ΤT
       related thereto
       Lahey, Thomas P., Laguna Niguel, CA, UNITED STATES
IN
       Rajadhyaksha, V.J., Mission Viejo, CA, UNITED STATES
       SynorX, Inc., San Clemente, CA, UNITED STATES, 92673 (U.S. corporation)
PA
PΙ
       US 2003069192
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## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ΑN
       2003:72168 USPATFULL
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       64 human secreted proteins
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Greene, John M., Gaithersburg, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Feng, Ping, Gaithersburg, MD, UNITED STATES
       Florence, Kimberly A., Rockville, MD, UNITED STATES
       Hu, Jing-Shan, Mountain View, CA, UNITED STATES
       Ferrie, Ann M., Tewksbury, MA, UNITED STATES
       Yu, Guo-Liang, Berkeley, CA, UNITED STATES
       Duan, Roxanne D., Bethesda, MD, UNITED STATES
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AN
TΙ
       186 human secreted proteins
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Carter, Kenneth C., North Potomac, MD, UNITED STATES
       Bednarik, Daniel P., Columbia, MD, UNITED STATES
       Endress, Gregory A., Florence, MA, UNITED STATES
       Yu, Guo-Liang, Berkeley, CA, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Feng, Ping, Gaithersburg, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Greene, John M., Gaithersburg, MD, UNITED STATES
       Ferrie, Ann M., Painted Post, NY, UNITED STATES
       Duan, D. Roxanne, Bethesda, MD, UNITED STATES
       Hu, Jing-Shan, Mountain View, CA, UNITED STATES
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Florence, Kimberly A., Rockville, MD, UNITED STATES
       Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
       Fischer, Carrie L., Burke, VA, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Brewer, Laurie A., St. Paul, MN, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       LaFleur, David W., Washington, DC, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Zeng, Zhizhen, Lansdale, PA, UNITED STATES
       Kyaw, Hla, Frederick, MD, UNITED STATES
PΙ
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DT FS

INCL

NCL

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L2
       2003:38352 USPATFULL
AN
ΤI
       143 human secreted proteins
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Komatsoulis, George A., Silver Spring, MD, UNITED STATES
       Birse, Charles E., North Potomac, MD, UNITED STATES
       Duan, Roxanne D., Bethesda, MD, UNITED STATES
       Florence, Kimberly A., Rockville, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
                               20030206
PI
       US 2003027999
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       US 2001-986480
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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     ANSWER 8 OF 52 USPATFULL
ΑN
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ΤI
       29 human cancer associated proteins
IN
       Roschke, Viktor, Rockville, MD, UNITED STATES
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       US 2003027776
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ΑI
       US 2001-23896
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L2
     ANSWER 9 OF 52 USPATFULL
       2003:30391 USPATFULL
ΑN
TI
       Kunitz-type protease inhibitor polynucleotides, polypeptides, and
       antibodies
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
```

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Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
PA
       corporation)
PΙ
       US 2003022338
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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AN
       2003:18018 USPATFULL
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       Composition, synthesis and therapeutic applications of polyamines
       Murphy, Michael A., La Jolla, CA, UNITED STATES
IN
       MaLachowski, Mitchell R., San Diego, CA, UNITED STATES
PΙ
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 11 OF 52 USPATFULL
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AN
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IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Chen, Lieping, Rochester, MN, UNITED STATES
       Baker, Kevin P., Darnestown, MD, UNITED STATES
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                                20021226
ΑI
       US 2001-790622
                          Α1
                                20010223 (9)
       Continuation-in-part of Ser. No. WO 2000-US23792, filed on 30 Aug 2000,
RLI
       UNKNOWN
PRAI
       US 1999-152317P
                           19990903 (60)
       US 2000-200346P
                           20000428 (60)
       Utility
DT
       APPLICATION
FS
LN.CNT 12424
INCL
       INCLM: 514/012.000
       INCLS: 435/069.100; 435/320.100; 435/325.000; 536/023.500
NCL
       NCLM: 514/012.000
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435/069.100; 435/320.100; 435/325.000; 536/023.500
IC
       [7]
       ICM: A61K038-17
       ICS: C12P021-02; C12N005-06; C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 12 OF 52 USPATFULL
L2
       2002:343975 USPATFULL
ΑN
       Serine protease polynucleotides, polypeptides, and antibodies
ΤI
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
PA
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
       corporation)
                               20021226
       US 2002197701
                          A1
PΙ
       US 2002-67761
                          Α1
                               20020208 (10)
ΑI
       Continuation of Ser. No. US 2001-804156, filed on 13 Mar 2001, PENDING
RLI
                           20000314 (60)
PRAI
       US 2000-189025P
DT
       Utility
       APPLICATION
LN.CNT 13077
INCL
       INCLM: 435/226.000
       INCLS: 435/069.100; 435/320.100; 435/325.000; 536/023.200
NCL
              435/226.000
              435/069.100; 435/320.100; 435/325.000; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12N009-64
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 13 OF 52 USPATFULL
L2
AN
       2002:337390 USPATFULL
TΙ
       Human polynucleotides, polypeptides, and antibodies
       Moore, Paul A., Germantown, MD, UNITED STATES
TN
       Coleman, Timothy A., Gaithersburg, MD, UNITED STATES
       Gentz, Reiner L., Rockville, MD, UNITED STATES
       Dillon, Patrick J., Carlsbad, CA, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Endress, Gregory A., Florence, MA, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
PΙ
       US 2002192749
                          Α1
                               20021219
ΑI
       US 2001-969384
                          A1
                               20011003 (9)
       Continuation-in-part of Ser. No. WO 2001-US10542, filed on 2 Apr 2001,
RLI
       UNKNOWN
PRAI
       US 2000-194118P
                           20000403 (60)
       US 2000-236384P
                           20000929 (60)
DT
       Utility
       APPLICATION
FS
LN.CNT 13925
       INCLM: 435/069.100
INCL
       INCLS: 435/183.000; 435/325.000; 435/320.100; 530/350.000; 536/023.200
              435/069.100
NCL
       NCLS:
              435/183.000; 435/325.000; 435/320.100; 530/350.000; 536/023.200
IC
       [7]
       ICM: C12P021-02
       ICS: C12N005-06; C07H021-04; C12N009-00; C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 14 OF 52 USPATFULL
L2
AN
       2002:322538 USPATFULL
TI
       ADAM polynucleotides, polypeptides, and antibodies
```

```
Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Hastings, Gregg A., Westlake Village, CA, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Wei, Ping, Brookeville, MD, UNITED STATES
       US 2002182702
                          Α1
                               20021205
PT
       US 2001-955504
                          A1
                                20010919 (9)
ΑI
       Continuation-in-part of Ser. No. WO 2000-US14308, filed on 25 May 2000,
RLI
       UNKNOWN Continuation-in-part of Ser. No. US 2000-712907, filed on 16 Nov
       2000, PENDING
PRAI
       US 2000-234222P
                            20000921 (60)
       US 1999-136388P
                            19990527 (60)
       US
       US
       US 1999-136388P
                            19990527 (60)
       US 1999-142930P
                            19990709 (60)
       US 2000-178717P
                            20000128 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 13921
       INCLM: 435/226.000
INCL
       INCLS: 435/325.000; 435/320.100; 435/069.100; 536/023.200
NCL
              435/226.000
              435/325.000; 435/320.100; 435/069.100; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12N009-64
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 15 OF 52 USPATFULL
AN
       2002:308509 USPATFULL
ΤI
       ADAM polynucleotides, polypeptides, and antibodies
TN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Hastings, Gregg A., Westlake Village, CA, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Wei, Ping, Brookeville, MD, UNITED STATES
PA
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES (U.S.
       corporation)
       US 2002173640
PI
                          Α1
                                20021121
ΑI
       US 2002-125452
                          A1
                                20020419 (10)
RLI
       Continuation of Ser. No. US 2001-955504, filed on 19 Sep 2001, PENDING
       Continuation of Ser. No. US 2000-712907, filed on 16 Nov 2000, PENDING
       Continuation of Ser. No. WO 2000-US14308, filed on 25 May 2000, UNKNOWN
PRAI
       US 2000-234222P
                            20000921 (60)
       US 1999-136388P
                            19990527 (60)
       US 1999-142930P
                            19990709 (60)
       US 2000-178717P
                           20000128 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 13925
INCL
       INCLM: 536/023.200
       INCLS: 435/226.000; 435/069.100; 435/325.000; 435/320.100
NCL
       NCLM:
              536/023.200
       NCLS:
              435/226.000; 435/069.100; 435/325.000; 435/320.100
IC
       [7]
       ICM: C07H021-04
       ICS: C12P021-06; C12N009-64; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 16 OF 52 USPATFULL
```

AN

2002:308333 USPATFULL

```
Protein tyrosine kinase receptor polynucleotides, polypeptides, and
TΙ
       antibodies
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
                                20021121
PΙ
       US 2002173458
                          Α1
ΑI
       US 2001-836392
                          Α1
                                20010418 (9)
       Continuation-in-part of Ser. No. WO 2000-US28066, filed on 12 Oct 2000,
RLI
       UNKNOWN
PRAI
       US 1999-159542P
                            19991015 (60)
       US 1999-165914P
                            19991117 (60)
       US 2000-189027P
                            20000314 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 13395
INCL
       INCLM: 514/012.000
       INCLS: 435/194.000; 435/325.000; 435/320.100; 435/069.100; 536/023.200
NCL
       NCLM: 514/012.000
              435/194.000; 435/325.000; 435/320.100; 435/069.100; 536/023.200
       NCLS:
IC
       [7]
       ICM: A61K038-17
       ICS: C07H021-04; C12N009-12; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 17 OF 52 USPATFULL
AN
       2002:307870 USPATFULL
ΤI
       28 human secreted proteins
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Zeng, Zhizhen, Lansdale, PA, UNITED STATES
       Kyaw, Hla, Frederick, MD, UNITED STATES
       Fischer, Carrie L., Burke, VA, UNITED STATES
       Li, Haodong, Gaithersburg, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Gentz, Reiner L., Rockville, MD, UNITED STATES
       Wei, Ying-Fei, Berkeley, CA, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Greene, John M., Gaithersburg, MD, UNITED STATES
       Ferrie, Ann M., Tewksbury, MA, UNITED STATES
PI
       US 2002172994
                          Α1
                                20021121
ΑI
       US 2001-852797
                          A1
                                20010511 (9)
RLI
       Continuation-in-part of Ser. No. US 1998-152060, filed on 11 Sep 1998,
       PENDING Continuation-in-part of Ser. No. WO 1998-US4858, filed on 12 Mar
       1998, UNKNOWN
       US 2001-265583P
                            20010202 (60)
PRAI
                            19970314 (60)
       US 1997-40762P
       US 1997-40710P
                            19970314 (60)
       US 1997-50934P
                            19970530 (60)
       US 1997-48100P
                            19970530 (60)
       US 1997-48357P
                            19970530 (60)
       US 1997-48189P
                            19970530 (60)
       US 1997-57765P
                            19970905
                                     (60)
                            19970606
       US 1997-48970P
                                     (60)
       US 1997-68368P
                            19971219 (60)
       Utility
DT
FS
       APPLICATION
LN.CNT 17794
INCL
       INCLM: 435/069.100
       INCLS: 435/226.000; 435/325.000; 435/320.100; 536/023.200
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NCLM:
              435/069.100
NCL.
       NCLS:
              435/226.000; 435/325.000; 435/320.100; 536/023.200
IC
       [7]
       ICM: C12P021-02
       ICS: C12N005-06; C07H021-04; C12N009-64
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 18 OF 52 USPATFULL
L2
AN
       2002:295334 USPATFULL
TΙ
       Steroid hormone receptor polynucleotides, polypeptides, and antibodies
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
PA
       corporation)
       US 2002165384
PΙ
                          A1
                                20021107
ΑI
       US 2002-103511
                          Α1
                                20020322 (10)
RLI
       Continuation of Ser. No. US 2001-805204, filed on 14 Mar 2001, PENDING
       Continuation-in-part of Ser. No. WO 2000-US24517, filed on 7 Sep 2000,
       UNKNOWN
                           20000314 (60)
       US 2000-189032P
PRAI
       US 1999-152932P
                           19990909 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 11571
       INCLM: 536/023.500
INCL
       INCLS: 530/350.000; 435/069.100; 435/320.100; 435/325.000
NCL
              536/023.500
       NCLS: 530/350.000; 435/069.100; 435/320.100; 435/325.000
       [7]
IC
       ICM: C07H021-04
       ICS: C07K014-72; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 19 OF 52 USPATFULL
AN
       2002:294650 USPATFULL
TI
       TM4SF receptor polynucleotides, polypeptides, and antibodies
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
PA
       Human Genome Sciences, Inc., Rockville, MD, 20850 (U.S. corporation)
PΙ
       US 2002164693
                               20021107
                          A1
       US 2001-972970
ΑI
                          A1
                                20011010 (9)
       Continuation-in-part of Ser. No. WO 2001-US11130, filed on 5 Apr 2001,
RLI
       UNKNOWN
PRAI
       US 2000-195336P
                           20000410 (60)
DT
       Utility
       APPLICATION
FS
LN.CNT 11940
       INCLM: 435/069.100
INCL
       INCLS: 435/325.000; 435/320.100; 435/006.000; 435/007.100; 530/350.000;
              536/023.500; 530/388.220
NCL
       NCLM:
              435/069.100
       NCLS:
              435/325.000; 435/320.100; 435/006.000; 435/007.100; 530/350.000;
              536/023.500; 530/388.220
IC
       ICM: C12Q001-68
       ICS: G01N033-53; C07H021-04; C12P021-02; C12N005-06; C07K014-715;
       C07K016-28
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 20 OF 52 USPATFULL
1.2
```

AN

2002:294649 USPATFULL

```
Immune system-related polynucleotides, polypeptides, and antibodies
TI
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Hilbert, David, Bethesda, MD, UNITED STATES
       Kenny, Joseph J., Damascus, MD, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Choi, Gil H., Rockville, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Gruber, Joachim R., Dallas, TX, UNITED STATES
       Endress, Gregory A., Florence, MA, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002164692
                          A1
                               20021107
ΑI
       US 2001-949842
                          A1
                               20010912 (9)
       Continuation-in-part of Ser. No. WO 2001-US7260, filed on 7 Mar 2001,
RLI
       UNKNOWN
                           20000308 (60)
PRAI
       US 2000-187873P
                           20000811 (60)
       US 2000-224367P
       Utility
DT
       APPLICATION
LN.CNT 13952
INCL
       INCLM: 435/069.100
       INCLS: 435/183.000; 435/320.100; 435/325.000; 536/023.200
NCL
              435/069.100
              435/183.000; 435/320.100; 435/325.000; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12N009-00
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 21 OF 52 USPATFULL
ΑN
       2002:287630 USPATFULL
       Serine/threonine phosphatase polynucleotides, polypeptides, and
TI
       antibodies
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
TN
       Ruben, Steven M., Olney, MD, UNITED STATES
                               20021031
PΤ
       US 2002160493
                          A1
                               20010830 (9)
ΑI
       US 2001-941831
                          Α1
       Continuation-in-part of Ser. No. WO 2001-US6256, filed on 28 Feb 2001,
RLI
       UNKNOWN
PRAI
       US 2000-186350P
                           20000302 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 14729
       INCLM: 435/226.000
INCL
       INCLS: 435/069.100; 435/325.000; 435/320.100; 536/023.200
NCL
       NCLM:
              435/226.000
              435/069.100; 435/325.000; 435/320.100; 536/023.200
       NCLS:
TC
       [7]
       ICM: C12N009-64
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 22 OF 52 USPATFULL
L2
AN
       2002:287628 USPATFULL
TТ
       Human Serpin polynucleotides, polypeptides, and antibodies
       Ni, Jian, Germantown, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
ΡI
       US 2002160491
                          Α1
                               20021031
ΑI
       US 2001-912628
                          Α1
                               20010726 (9)
RLI
       Continuation-in-part of Ser. No. WO 2000-US5082, filed on 29 Feb 2000,
       UNKNOWN Continuation-in-part of Ser. No. WO 2001-US2484, filed on 26 Jan
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2001, UNKNOWN
PRAI
       US 2000-178769P
                            20000128 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 12380
INCL
       INCLM: 435/226.000
       INCLS: 435/069.100; 435/325.000; 435/320.100; 536/023.200
NCL
              435/226.000
              435/069.100; 435/325.000; 435/320.100; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12N009-64
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 23 OF 52 USPATFULL
AN
       2002:272888 USPATFULL
ΤI
       Human polynucleotides, polypeptides, and antibodies
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PA
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
       corporation)
       US 2002151009
PΙ
                          Α1
                                20021017
ΑI
       US 2001-939825
                          Α1
                                20010828 (9)
RLI
       Continuation-in-part of Ser. No. WO 2001-US5498, filed on 22 Feb 2001,
       UNKNOWN
PRAI
       US 2000-184664P
                            20000224 (60)
       US 2000-189874P
                            20000316 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 14831
INCL
       INCLM: 435/183.000
       INCLS: 435/006.000; 435/069.100; 435/325.000; 435/320.100; 536/023.200
NCL
              435/183.000
       NCLS:
              435/006.000; 435/069.100; 435/325.000; 435/320.100; 536/023.200
IC
       [7]
       ICM: C12N009-00
       ICS: C120001-68; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 24 OF 52 USPATFULL
L_2
AN
       2002:221965 USPATFULL
TI
       Steroid hormone receptor polynucleotides, polypeptides, and antibodies
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002120110
                                20020829
                          Α1
                                20010314 (9)
ΑI
       US 2001-805204
                          A1
       Continuation-in-part of Ser. No. WO 2000-US24517, filed on 7 Sep 2000,
RLI
       UNKNOWN
PRAI
       US 2000-189032P
                           20000314 (60)
       Utility
DТ
       APPLICATION
FS
LN.CNT 11573
INCL
       INCLM: 536/023.100
       INCLS: 530/350.000; 530/387.100
NCL
       NCLM:
              536/023.100
       NCLS:
              530/350.000; 530/387.100
IC
       [7]
       ICM: C07H021-02
       ICS: C07H021-04; C07K001-00; C07K014-00; C07K017-00; C07K016-00
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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T.2
     ANSWER 25 OF 52 USPATFULL
       2002:221958 USPATFULL
AN
ΤI
       17 human secreted proteins
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Komatsoulis, George A., Silver Spring, MD, UNITED STATES
       Baker, Kevin P., Darnestown, MD, UNITED STATES
       Birse, Charles E., North Potomac, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Wei, Ping, Brookeville, MD, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Duan, D. Roxanne, Bethesda, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Choi, Gil H., Rockville, MD, UNITED STATES
       Fiscella, Michele, Bethesda, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       Barash, Steven C., Rockville, MD, UNITED STATES
ΡI
                                20020829
       US 2002120103
                          Α1
ΑI
       US 2001-915582
                          Α1
                                20010727 (9)
RLI
       Continuation-in-part of Ser. No. WO 2001-US1431, filed on 17 Jan 2001,
       UNKNOWN
                           20000131 (60)
PRAI
       US 2000-179065P
       US 2000-180628P
                           20000204 (60)
       US 2000-231968P
                           20000912 (60)
DT
       Utility
       APPLICATION
FS
LN.CNT 20680
       INCLM: 530/350.000
INCL
       INCLS: 536/023.500; 514/012.000; 435/069.100; 435/325.000; 435/320.100;
              435/006.000; 530/388.100
NCL
       NCLM:
              530/350.000
       NCLS:
              536/023.500; 514/012.000; 435/069.100; 435/325.000; 435/320.100;
              435/006.000; 530/388.100
IC
       [7]
       ICM: C12Q001-68
       ICS: C07K014-435; C07H021-04; A61K038-17; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 26 OF 52 USPATFULL
L2
       2002:221379 USPATFULL
AN
ΤI
       Trefoil domain-containing polynucleotides, polypeptides, and antibodies
IN
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002119519
                                20020829
                          Α1
AΙ
       US 2001-891171
                          Α1
                                20010626 (9)
       Continuation-in-part of Ser. No. WO 2000-US34920, filed on 22 Dec 2000,
RLI
       UNKNOWN
PRAI
       US 1999-171618P
                           19991223 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 12171
INCL
       INCLM: 435/069.100
       INCLS: 435/183.000; 435/320.100; 435/325.000; 536/023.200
NCL
       NCLM:
              435/069.100
       NCLS:
              435/183.000; 435/320.100; 435/325.000; 536/023.200
IC
       ICM: C07H021-04
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ICS: C12N009-00; C12P021-02; C12N005-06 CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 27 OF 52 USPATFULL L2 ΑN 2002:198680 USPATFULL Extracellular matrix polynucleotides, polypeptides, and antibodies ΤI TN Fiscella, Michele, Bethesda, MD, UNITED STATES Ebner, Reinhard, Gaithersburg, MD, UNITED STATES Shi, Yanggu, Gaithersburg, MD, UNITED STATES Ruben, Steven M., Olney, MD, UNITED STATES 20020808 PΙ US 2002106780 Α1 ΑI US 2001-978249 Α1 20011017 (9) Continuation-in-part of Ser. No. WO 2001-US11643, filed on 11 Apr 2001, RLI UNKNOWN 20000418 (60) PRAI US 2000-198123P Utility DT FS APPLICATION LN.CNT 13488 INCL INCLM: 435/226.000 INCLS: 435/069.100; 435/006.000; 435/325.000; 435/320.100; 536/023.200 NCL 435/226.000 435/069.100; 435/006.000; 435/325.000; 435/320.100; 536/023.200 IC [7] ICM: C12N009-64 ICS: C12Q001-68; C07H021-04; C12P021-02; C12N005-06 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L2 ANSWER 28 OF 52 USPATFULL AN 2002:198631 USPATFULL ΤI Bcl-2-like polynucleotides, polypeptides, and antibodies Ruben, Steven M., Olney, MD, UNITED STATES IN Duan, D. Roxanne, Bethesda, MD, UNITED STATES Ni, Jian, Germantown, MD, UNITED STATES PΙ US 2002106731 A1 20020808 20010726 (9) ΑI US 2001-912599 Α1 Continuation-in-part of Ser. No. WO 2001-US3080, filed on 31 Jan 2001, RLI UNKNOWN PRAI US 2000-179487P 20000201 (60) 20000207 (60) US 2000-180697P DTUtility FS APPLICATION LN.CNT 12354 INCL INCLM: 435/069.100 INCLS: 435/006.000; 435/007.230; 435/325.000; 435/320.100; 536/023.200 NCL 435/069.100 NCLS: 435/006.000; 435/007.230; 435/325.000; 435/320.100; 536/023.200 IC [7] ICM: C12P021-02 ICS: C12Q001-68; G01N033-574; C07H021-04 CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 29 OF 52 USPATFULL L2 2002:179165 USPATFULL ANTI Plasminogen-like polynucleotides, polypeptides, and antibodies IN Ni, Jian, Germantown, MD, UNITED STATES Young, Paul E., Gaithersburg, MD, UNITED STATES Ruben, Steven M., Olney, MD, UNITED STATES PΙ US 2002094955 A1 20020718 ΑI US 2001-832197 A1 20010411 (9)

Continuation-in-part of Ser. No. WO 2000-US27253, filed on 4 Oct 2000,

19991007 (60)

RLI

PRAI

UNKNOWN

US 1999-158044P

```
DT
       Utility
       APPLICATION
FS
LN.CNT 11038
INCL
       INCLM: 514/012.000
       INCLS: 536/023.200; 435/320.100; 435/325.000; 435/183.000
              514/012.000
NCL
       NCLS: 536/023.200; 435/320.100; 435/325.000; 435/183.000
IC
       [7]
       ICM: A61K038-17
       ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
T.2
     ANSWER 30 OF 52 USPATFULL
AN
       2002:171946 USPATFULL
       Kunitz-type protease inhibitor polynucleotides, polypeptides, and
TI
       antibodies
ΤN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       US 2002090695
                               20020711
PΙ
                          Α1
       US 2001-858718
                          Α1
                                20010517 (9)
ΑI
       Continuation-in-part of Ser. No. WO 2000-US31917, filed on 21 Nov 2000,
RLI
       UNKNOWN
PRAI
       US 1999-166751P
                           19991122 (60)
DT
       Utility
       APPLICATION
FS
LN.CNT 12006
INCL
       INCLM: 435/184.000
       INCLS: 435/069.200; 435/325.000; 435/320.100; 536/023.200
NCL
              435/184.000
       NCLM:
              435/069.200; 435/325.000; 435/320.100; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12N009-99
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 31 OF 52 USPATFULL
AN
       2002:157008 USPATFULL
TI
       Four disulfide core domain-containing (FDCD) polynucleotides,
       polypeptides, and antibodies
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       US 2002081607
                                20020627
PT
                          Α1
                                20010606 (9)
ΑI
       US 2001-874062
                          A1
       Continuation-in-part of Ser. No. WO 2000-US32462, filed on 29 Nov 2000,
RLI
PRAI
       US 1999-168229P
                            19991201 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 11572
       INCLM: 435/006.000
INCL
       INCLS: 435/007.100; 435/069.100; 435/325.000; 536/023.500; 530/350.000
NCL
       NCLM:
              435/006.000
              435/007.100; 435/069.100; 435/325.000; 536/023.500; 530/350.000
       NCLS:
IC
       [7]
       ICM: C12Q001-68
       ICS: G01N033-53; C07H021-04; C07K014-435; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 32 OF 52 USPATFULL
L2
AN
       2002:149306 USPATFULL
ΤI
       ADAM polynucleotides, polypeptides, and antibodies
IN
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
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Ruben, Steven M., Olney, MD, UNITED STATES
       US 2002077465
                          A1
                               20020620
PΙ
AI
       US 2001-945676
                          A1
                               20010905 (9)
       Continuation-in-part of Ser. No. WO 2001-US5497, filed on 22 Feb 2001,
RLI
       UNKNOWN
PRAI
       US 2000-187937P
                           20000303 (60)
       Utility
DТ
FS
       APPLICATION
LN.CNT 12287
INCL
       INCLM: 536/023.200
       INCLS: 435/320.100; 435/325.000; 435/069.100; 435/183.000
NCL
              536/023.200
              435/320.100; 435/325.000; 435/069.100; 435/183.000
       NCLS:
IC
       [7]
       ICM: C07H021-04
       ICS: C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 33 OF 52 USPATFULL
L2
AN
       2002:149299 USPATFULL
TI
       Death domain-containing receptor polynucleotides, polypeptides, and
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       US 2002077458
                               20020620
PΙ
                          Α1
                               20010417 (9)
ΑI
       US 2001-835788
                          Α1
RLI
       Continuation-in-part of Ser. No. WO 2000-US28666, filed on 17 Oct 2000,
       UNKNOWN
PRAI
       US 1999-159585P
                           19991018 (60)
       US 1999-167246P
                           19991124 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 14143
INCL
       INCLM: 530/350.000
       INCLS: 536/023.500; 435/320.100; 435/325.000; 435/069.100; 530/324.000;
              530/387.900; 514/044.000; 435/006.000; 435/007.100; 514/002.000
NCL
       NCLM:
              530/350.000
              536/023.500; 435/320.100; 435/325.000; 435/069.100; 530/324.000;
       NCLS:
              530/387.900; 514/044.000; 435/006.000; 435/007.100; 514/002.000
IC
       [7]
       ICM: A01N037-18
       ICS: A61K038-00; C12Q001-68; G01N033-53; C07H021-04; A61K031-70;
       A01N043-04; C12P021-06; C12N015-00; C12N015-09; C12N015-63; C12N015-70;
       C12N015-74; C07K005-00; C07K007-00; C07K016-00; C07K017-00; C12N005-00;
       C12N005-02; C07K001-00; C07K014-00; C12P021-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 34 OF 52 USPATFULL
L2
ΑN
       2002:149131 USPATFULL
ΤI
       28 human secreted proteins
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Zeng, Zhizhen, Lansdale, PA, UNITED STATES
       Kyaw, Hla, Frederick, MD, UNITED STATES
       Fischer, Carrie L., Burke, VA, UNITED STATES
       Li, Haodong, Gaithersburg, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Gentz, Reiner L., Rockville, MD, UNITED STATES
       Wei, Ying-Fei, Berkeley, CA, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
```

Young, Paul E., Gaithersburg, MD, UNITED STATES

```
Greene, John M., Gaithersburg, MD, UNITED STATES
       Ferrie, Ann M., Tewksbury, MA, UNITED STATES
PΙ
       US 2002077287
                          Α1
                                20020620
ΑI
       US 2001-852659
                          ·A1
                                20010511 (9)
       Continuation-in-part of Ser. No. US 1998-152060, filed on 11 Sep 1998,
RLI
       UNKNOWN
DT
       Utility
       APPLICATION
FS
LN.CNT 17779
INCL
       INCLM: 514/012.000
       INCLS: 435/325.000; 435/320.100; 435/069.100; 435/183.000; 530/350.000;
              536/023.200
NCL
       NCLM:
              514/012.000
       NCLS:
              435/325.000; 435/320.100; 435/069.100; 435/183.000; 530/350.000;
              536/023.200
IC
       [7]
       ICM: A61K038-17
       ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06; C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 35 OF 52 USPATFULL
L2
AN
       2002:148614 USPATFULL
ΤI
       28 human secreted proteins
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Zeng, ZhiZhen, Lansdale, PA, UNITED STATES
       Kyaw, Hla, Frederick, MD, UNITED STATES
       Fischer, Carrie L., Burke, VA, UNITED STATES
       Li, Haodong, Gaithersburg, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Gentz, Reiner L., Rockville, MD, UNITED STATES
       Wei, Ying-Fei, Berkeley, CA, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Greene, John M., Gaithersburg, MD, UNITED STATES
       Ferrie, Ann M., Painted Post, NY, UNITED STATES
PΙ
       US 2002076756
                          Α1
                               20020620
ΑI
       US 2001-853161
                          A1
                                20010511 (9)
PRAI
       US 2001-265583P
                           20010202 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 17788
INCL
       INCLM: 435/069.100
       INCLS: 435/325.000; 435/320.100; 530/350.000; 536/023.500
NCL
              435/069.100
       NCLM:
              435/325.000; 435/320.100; 530/350.000; 536/023.500
       NCLS:
IC
       [7]
       ICM: C12P021-02
       ICS: C12N005-06; C07H021-04; C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 36 OF 52 USPATFULL
       2002:141609 USPATFULL
ΑN
TΙ
       Transferrin polynucleotides, polypeptides, and antibodies
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
                               20020613
       US 2002072596
PΙ
                          Α1
       US 2001-891126
                          Α1
                               20010626 (9)
ΑI
       Continuation-in-part of Ser. No. WO 2000-US34769, filed on 21 Dec 2000,
RLI
       UNKNOWN
       US 1999-171595P
PRAI
                           19991223 (60)
```

```
DT
       Utility
       APPLICATION
FS
LN.CNT 12048
INCL
       INCLM: 536/023.500
       INCLS: 530/350.000; 435/069.100; 435/325.000; 435/320.100
NCL
              536/023.500
       NCLM:
       NCLS: 530/350.000; 435/069.100; 435/325.000; 435/320.100
IC
       [7]
       ICM: C07H021-04
       ICS: C07K014-705; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 37 OF 52 USPATFULL
AN
       2002:133469 USPATFULL
       Serine protease polynucleotides, polypeptides, and antibodies
ТΙ
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
                               20020606
PΙ
       US 2002068320
                          A1
ΑI
       US 2001-804156
                          A1
                                20010313 (9)
PRAI
       US 2000-189025P
                           20000314 (60)
       Utility
FS
       APPLICATION
LN.CNT 13119
       INCLM: 435/069.100
TNCL
       INCLS: 435/226.000; 435/325.000; 435/006.000; 435/007.100; 530/388.100;
              536/023.200
NCL
       NCLM:
              435/069.100
              435/226.000; 435/325.000; 435/006.000; 435/007.100; 530/388.100;
       NCLS:
              536/023.200
IC
       [7]
       ICM: C12Q001-68
       ICS: G01N033-53; C12P021-02; C12N005-06; C07H021-04; C12N009-64
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 38 OF 52 USPATFULL
T.2
AN
       2002:126703 USPATFULL
ΤI
       Immunoglobulin superfamily polynucleotides, polypeptides, and antibodies
IN
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Ni, Jain, Rockville, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
PΙ
       US 2002065220
                          A1
                                20020530
                                20010307 (9)
ΑI
       US 2001-799514
                          A1
       Continuation-in-part of Ser. No. WO 2000-US23662, filed on 29 Aug 2000,
RLI
       UNKNOWN
PRAI
       US 1999-152248P
                           19990903 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 12437
       INCLM: 514/012.000
INCL
       INCLS: 536/023.100; 435/069.100; 435/325.000; 435/320.100
NCL
              514/012.000
       NCLM:
              536/023.100; 435/069.100; 435/325.000; 435/320.100
       NCLS:
IC
       [7]
       ICM: A61K038-17
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 39 OF 52 USPATFULL
L2
AN
       2002:126332 USPATFULL
```

Human protein tyrosine phosphatase polynucleotides, polypeptides, and

TI

```
antibodies
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002064844
                          Α1
                               20020530
ΑI
       US 2001-906779
                               20010718 (9)
                          Α1
       Continuation-in-part of Ser. No. WO 2001-US1563, filed on 17 Jan 2001,
RLI
       UNKNOWN
       US 2000-176306P
                           20000118 (60)
PRAI
DT
       Utility
FS
       APPLICATION
LN.CNT 12129
INCL
       INCLM: 435/183.000
       INCLS: 435/006.000; 435/069.100; 435/325.000; 435/320.100; 536/023.200
              435/183.000
NCL
       NCLS:
              435/006.000; 435/069.100; 435/325.000; 435/320.100; 536/023.200
IC
       [7]
       ICM: C12N009-00
       ICS: C12Q001-68; C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 40 OF 52 USPATFULL
AN
       2002:126314 USPATFULL
ΤI
       Cytokine receptor-like polynucleotides, polypeptides, and antibodies
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
                               20020530
PΤ
       US 2002064826
                          Α1
                          Α1
                               20010606 (9)
ΑI
       US 2001-874069
       Continuation-in-part of Ser. No. WO 2000-US32525, filed on 30 Nov 2000,
RLI
       UNKNOWN
PRAI
       US 1999-168621P
                           19991203 (60)
DΤ
       Utility
       APPLICATION
FS
LN.CNT 12089
INCL
       INCLM: 435/069.100
       INCLS: 435/325.000; 435/320.100; 536/023.100
NCL
       NCLM:
              435/069.100
       NCLS:
              435/325.000; 435/320.100; 536/023.100
IC
       [7]
       ICM: C07H021-02
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 41 OF 52 USPATFULL
L2
AN
       2002:126306 USPATFULL
ΤI
       52 human secreted proteins
       Ni, Jian, Germantown, MD, UNITED STATES
TN
       Baker, Kevin P., Darnestown, MD, UNITED STATES
       Birse, Charles E., North Potomac, MD, UNITED STATES
       Fiscella, Michele, Bethesda, MD, UNITED STATES
       Komatsoulis, George A., Silver Spring, MD, UNITED STATES
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Duan, D. Roxanne, Bethesda, MD, UNITED STATES
       Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
       LaFleur, David W., Washington, DC, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
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Wei, Ping, Brookeville, MD, UNITED STATES

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Florence, Kimberly A., Rockville, MD, UNITED STATES
ΡI
       US 2002064818
                          Α1
                                20020530
ΑI
       US 2001-789561
                          Α1
                                20010222 (9)
       Continuation-in-part of Ser. No. WO 2000-US24008, filed on 31 Aug 2000,
RLI
       UNKNOWN
PRAI
       US 1999-152317P
                            19990903 (60)
       US 1999-152315P
                            19990903 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 24623
INCL
       INCLM: 435/069.100
       INCLS: 435/006.000; 435/007.100; 536/023.100; 435/325.000
NCL
       NCLM:
              435/069.100
              435/006.000; 435/007.100; 536/023.100; 435/325.000
       NCLS:
IC
       [7]
       ICM: C12P021-02
       ICS: C12Q001-68; G01N033-53; C07H021-04; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 42 OF 52 USPATFULL
L2
ΑN
       2002:119846 USPATFULL
ΤI
       Human G-protein Chemokine receptor (CCR5) HDGNR10
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Roschke, Viktor, Rockville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       US 2002061834
                               20020523
PΤ
                          Α1
       US 2001-779880
                               20010209 (9)
ΑI
                          Α1
PRAI
       US 2000-181258P
                           20000209 (60)
       US 2000-187999P
                           20000309 (60)
       US 2000-234336P
                           20000922 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 18667
INCL
       INCLM: 514/001.000
       INCLS: 530/350.000; 536/023.500; 435/325.000; 435/320.100; 435/069.100
NCL
       NCLM:
              514/001.000
       NCLS:
              530/350.000; 536/023.500; 435/325.000; 435/320.100; 435/069.100
IC
       [7]
       ICM: A61K031-00
       ICS: C07H021-04; C07K014-705; C12N005-06; C12P021-02
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 43 OF 52 USPATFULL
       2002:105937 USPATFULL
AN
       Major intrinsic protein (MIP)-like polynucleotides, polypeptides, and
TI
       antibodies
IN
       Ruben, Steven A., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
PA
       Human Genome Sciences, Inc., Rockville, MD (U.S. corporation)
PΙ
       US 2002055142
                          A1
                               20020509
ΑI
       US 2001-862419
                          Α1
                                20010523 (9)
RLI
       Continuation-in-part of Ser. No. WO 2000-US31919, filed on 21 Nov 2000,
       UNKNOWN
PRAI
       US 1999-167247P
                           19991124 (60)
       Utility
DT
FS
       APPLICATION
LN.CNT 11747
INCL
       INCLM: 435/069.100
       INCLS: 536/023.500; 435/320.100; 435/325.000; 530/324.000; 530/387.900;
              435/006.000; 435/007.200
NCL
              435/069.100
       NCLM:
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536/023.500; 435/320.100; 435/325.000; 530/324.000; 530/387.900;
       NCLS:
              435/006.000; 435/007.200
IC
       [7]
       ICM: C12Q001-68
       ICS: G01N033-53; G01N033-567; C07H021-04; C12P021-06; C12N015-00;
       C12N015-09; C12N015-63; C12N015-70; C12N015-74; C07K005-00; C07K007-00;
       C07K016-00; C07K017-00; A61K038-00; C12N005-00; C12N005-02; C12P021-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 44 OF 52 USPATFULL
L2
       2002:99088 USPATFULL
AN
       Kringle domain-containing polynucleotides, polypeptides, and antibodies
ΤI
       Ni, Jian, Germantown, MD, UNITED STATES
IN
       Moore, Paul A., Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
                               20020502
PΙ
       US 2002051984
                          A1
       US 2001-848288
                          A1
                               20010504 (9)
ΑI
       Continuation-in-part of Ser. No. WO 2000-US30664, filed on 8 Nov 2000,
RLI
       UNKNOWN
       US 1999-164853P
                           19991112 (60)
PRAI
DT
       Utility
FS
       APPLICATION
LN.CNT 12041
       INCLM: 435/006.000
INCL
       INCLS: 536/023.100; 435/007.100; 435/069.100; 514/044.000; 514/012.000;
              435/183.000; 530/350.000
NCL
              435/006.000
       NCLM:
              536/023.100; 435/007.100; 435/069.100; 514/044.000; 514/012.000;
       NCLS:
              435/183.000; 530/350.000
IC
       ICM: A61K048-00
       ICS: C07K014-435; A61K038-17; C12P021-02; C12Q001-68; G01N033-53;
       C12N009-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 45 OF 52 USPATFULL
AN
       2002:92268 USPATFULL
ΤI
       Human G-protein Chemokine Receptor HDGNR10
IN
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
       Roschke, Viktor, Rockville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       US 2002048786
                               20020425
PΙ
                          A1
ΑI
       US 2001-779879
                          Α1
                               20010209 (9)
       US 2000-181258P
                           20000209 (60)
PRAI
       US 2000-187999P
                           20000309 (60)
                           20000922 (60)
       US 2000-234336P
DT
       Utility
       APPLICATION
FS
LN.CNT 17969
       INCLM: 435/069.100
INCL
       INCLS: 536/023.500; 424/130.100; 514/012.000; 435/007.200; 435/325.000
              435/069.100
NCL
       NCLM:
              536/023.500; 424/130.100; 514/012.000; 435/007.200; 435/325.000
       NCLS:
IC
       [7]
       ICM: G01N033-53
       ICS: G01N033-567; A61K038-00; C07H021-04; C12P021-06; A61K039-395;
       C12N005-02; C12N005-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
1.2
     ANSWER 46 OF 52 USPATFULL
ΑN
       2002:88529 USPATFULL
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ΤI
       Metforimin-containing compositions for the treatment of diabetes
IN
       Fine, Stuart A., Northbrook, IL, United States
       Kinsella, Kevin J., La Jolla, CA, United States
PA
       Akesis Pharmaceuticals, Inc., La Jolla, CA, United States (U.S.
       corporation)
PΤ
       US 6376549
                          В1
                                20020423
       US 1998-156102
                                19980917 (9)
ΑI
       Utility
DT
FS
       GRANTED
LN.CNT 1429
INCL
       INCLM: 514/635.000
       INCLS: 424/617.000; 424/626.000; 424/639.000; 424/655.000
NCL
              514/635.000
              424/617.000; 424/626.000; 424/639.000; 424/655.000
       NCLS:
IC
       [7]
       ICM: A61K031-55
       ICS: A61K033-24; A61K033-22; A01N059-22
       424/646; 424/655; 424/682; 514/25; 514/162; 514/249; 514/255; 514/315;
EXF
       514/331; 514/439; 514/440; 514/458; 514/592; 514/593; 514/635; 514/866
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 47 OF 52 USPATFULL
L_2
ΑN
       2002:78715 USPATFULL
TI
       Stanniocalcin polynucleotides, polypeptides, and methods based thereon
IN
       Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
       Zhang, Ke-Zhou, Brussels, BELGIUM
       Lindsberg, Perttu, Helsinki, FINLAND
       Tatlisumak, Turgut, Helsinki, FINLAND
       Kaste, Markku, Vantaa, FINLAND
       Andersson, Leif C., Helsinki, FINLAND
PΑ
       Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
       corporation)
PΤ
       US 2002042372
                                20020411
                          Α1
ΑI
       US 2001-840989
                          Α1
                                20010425 (9)
RLI
       Continuation-in-part of Ser. No. WO 2000-US29432, filed on 26 Oct 2000,
       UNKNOWN
PRAI
       US 1999-161740P
                           19991027 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 9559
INCL
       INCLM: 514/012.000
       INCLS: 424/145.100; 530/388.240
NCL
       NCLM: 514/012.000
       NCLS:
              424/145.100; 530/388.240
IC
       [7]
       ICM: A61K038-22
       ICS: A61K039-395; C07K016-26
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 48 OF 52 USPATFULL
L2
AN
       2002:66870 USPATFULL
ΤI
       IL-6-like polynucleotides, polypeptides, and antibodies
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       US 2002037523
PΤ
                          Α1
                               20020328
ΑI
       US 2001-875016
                          Α1
                                20010607 (9)
       Continuation-in-part of Ser. No. WO 2000-US33134, filed on 7 Dec 2000,
RLI
       UNKNOWN
PRAI
       US 1999-169838P
                           19991209 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 11587
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INCL
       INCLM: 435/006.000
       INCLS: 536/023.500; 435/007.100; 435/069.520; 435/320.100; 435/325.000;
              530/351.000; 424/085.200
NCL
       NCLM:
              435/006.000
       NCLS:
              536/023.500; 435/007.100; 435/069.520; 435/320.100; 435/325.000;
              530/351.000; 424/085.200
IC
       [7]
       ICM: C12Q001-68
       ICS: G01N033-53; C07H021-04; C12P021-04; A61K038-20; C12N005-06;
       C07K014-54
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 49 OF 52 USPATFULL
AN
       2002:12261 USPATFULL
       Uteroglobin-like polynucleotides, polypeptides, and antibodies
ΤI
IN
       Ni, Jian, Germantown, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
                                20020117
PΙ
       US 2002006640 ,
                          A1
                                20010502 (9)
ΑI
       US 2001-846258
                          Α1
       Continuation-in-part of Ser. No. WO 2000-US30326, filed on 3 Nov 2000,
RLI
       UNKNOWN
PRAI
       US 1999-163395P
                            19991104 (60)
       Utility
DT
FS
       APPLICATION
LN.CNT 12076
TNCL
       INCLM: 435/069.100
       INCLS: 435/325.000; 435/006.000; 435/007.100; 514/044.000; 530/350.000;
              536/023.500
NCL
       NCLM:
              435/069.100
       NCLS:
              435/325.000; 435/006.000; 435/007.100; 514/044.000; 530/350.000;
              536/023.500
IC
       [7]
       ICM: C12P021-02
       ICS: C12N005-06; A61K048-00; C07K014-72; C12Q001-68; G01N033-53;
       C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L2
     ANSWER 50 OF 52 USPATFULL
       2002:8489 USPATFULL
AN
ΤT
       Retinoid receptor interacting polynucleotides, polypeptides, and
       antibodies
IN
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
       US 2002004489
                                20020110
PΙ
                          A1
ΑI
       US 2001-788600
                          A1
                                20010221 (9)
       Continuation-in-part of Ser. No. WO 2000-US22351, filed on 15 Aug 2000,
RLI
       UNKNOWN
PRAI
       US 1999-148757P
                            19990816 (60)
       US 2000-189026P
                            20000314 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 11257
       INCLM: 514/044.000
INCL
       INCLS: 536/023.500; 530/350.000; 435/069.100; 435/325.000; 530/388.220
NCL .
       NCLM:
              514/044.000
              536/023.500; 530/350.000; 435/069.100; 435/325.000; 530/388.220
       NCLS:
IC
       [7]
       ICM: A61K048-00
       ICS: C07H021-04; C12P021-02; C12N005-06; C07K014-705; C07K016-28
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

ANSWER 51 OF 52 USPATFULL

L2

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2001:40034 USPATFULL
AN
ΤI
       Dietary supplement and method of treatment for diabetic control
IN
       Fine, Stuart A., Northbrook, IL, United States
       Akesis Pharmaceuticals, Inc., San Diego, CA, United States (U.S.
PA
       corporation)
PΙ
       US 6203819
                          В1
                               20010320
       US 1999-272819
AΤ
                               19990319 (9)
       Continuation of Ser. No. US 1997-964814, filed on 5 Nov 1997
RLI
PRAI
       US 1997-39958P
                           19970307 (60)
DT
       Utility
FS
       Granted
LN.CNT 1275
INCL
       INCLM: 424/646.000
       INCLS: 424/655.000; 424/681.000; 424/682.000; 514/165.000; 514/458.000
NCL
       NCLM: 424/646.000
       NCLS: 424/655.000; 424/681.000; 424/682.000; 514/165.000; 514/458.000
IC
       [7]
       ICM: A61K033-26
       ICS: A61K033-24; A61K033-14; A61K031-60; A61K031-355
       424/646; 424/655; 424/681; 424/682; 514/165; 514/458
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 52 OF 52 USPATFULL
L2
AN
       1999:120934 USPATFULL
ΤI
       Dietary supplement and method of treatment for diabetic control
       Fine, Stuart A., Northbrook, IL, United States
TN
       Akesis Pharmaceuticals, Inc., La Jolla, CA, United States (U.S.
PA
       corporation)
PΙ
       US 5962030
                               19991005
ΑI
       US 1997-964814
                               19971105 (8)
       US 1997-39958P
PRAI
                           19970307 (60)
DT
       Utility
FS
       Granted
LN.CNT 1156
INCL
       INCLM: 424/646.000
       INCLS: 424/655.000; 424/681.000; 424/682.000; 514/165.000
NCL
       NCLM: 424/646.000
       NCLS: 424/655.000; 424/681.000; 424/682.000; 514/165.000
IC
       [6]
       ICM: A61K033-26
       ICS: A61K033-24; A61K033-14; A61K033-06; A61K031-60
       424/646; 424/655; 424/681; 424/682; 514/165
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
=>
=> d 12 44-54 kwic, bib
     ANSWER 44 OF 52 USPATFULL
         . . and increases clearance due to the aggregate's immunogenic
SUMM
       activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967);
       Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al.,
       Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993)).
SUMM
         . . thrombocytopenia, idiopathic thrombocytopenia purpura, purpura
       (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's
       syndrome, 5Pemphigus vulgaris, myasthenia gravis, Grave's disease
       (hyperthyroidism), and insulin-resistant diabetes mellitus.
SUMM
         . . polychondritis, rheumatic heart disease, neuritis, uveitis
       ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome,
       autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome,
```

insulin dependent diabetes mellitus, and autoimmune

inflammatory eye disorders.

SUMM . . . and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone ANA (SS-B)), diabetes mellitus (often characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with. . .

SUMM . . . characterized by inflammation (e.g., hepatitis, rheumatoid arthritis, gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant rejection).

SUMM . . . autoimmune and chronic inflammatory and infective diseases. Examples of autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.

SUMM . . . hypochromic anemia, microcytic anemia, chlorosis, hereditary siderob; astic anemia, idiopathic acquired sideroblastic anemia, red cell aplasia, megaloblastic anemia (e.g., pernicious anemia, (vitamin B12 deficiency) and folic acid deficiency anemia), aplastic anemia, hemolytic anemias (e.g., autoimmune helolytic anemia, microangiopathic hemolytic anemia, and paroxysmal. . .

SUMM . . . are not limited to, infantile genetic agranulocytosis, familial neutropenia, cyclic neutropenia, neutropenias resulting from or associated with dietary deficiencies (e.g., vitamin B 12 deficiency or folic acid deficiency), neutropenias resulting from or associated with drug treatments (e.g., antibiotic regimens such as. .

SUMM . . . treat metabolic and congenital disorders of the kidney (e.g., uremia, renal amyloidosis, renal osteodystrophy, renal tubular acidosis, renal glycosuria, nephrogenic diabetes insipidus, cystinuria, Fanconi's syndrome, renal fibrocystic osteosis (renal rickets), Hartnup disease, Bartter's syndrome, Liddle's syndrome, polycystic kidney disease, medullary cystic disease, medullary sponge kidney, Alport's syndrome, nail-patella syndrome, congenital nephrotic syndrome, CRUSH syndrome, horseshoe kidney, diabetic nephropathy, nephrogenic diabetes insipidus, analgesic nephropathy, kidney stones, and membranous nephropathy), and autoimmune disorders of the kidney (e.g., systemic lupus erythematosus (SLE), Goodpasture. . .

SUMM . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

SUMM . . . venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as. . .

SUMM . . . polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of **diabetes** mellitus. In patients with newly diagnosed Types I and II **diabetes**, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could. . .

SUMM . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B 12 deficiency, folic acid deficiency, Wernicke disease, tobacco- alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;

- (8) lesions caused by toxic substances including alcohol, lead, or.
- SUMM [0650] Endocrine system and/or hormone imbalance disorders and/or diseases include disorders and/or diseases of the pancreas, such as, for example, diabetes mellitus, diabetes insipidus, congenital pancreatic agenesis, pheochromocytoma—islet cell tumor syndrome; disorders and/or diseases of the adrenal glands such as, for example, Addison's. . .
- SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type I diabetes mellitus (insulin dependent diabetes mellitus, IDDM).
- SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type II diabetes mellitus (insulin resistant diabetes mellitus).
- SUMM . . . antagonistic antibodies) may be used to diagnose, prognoses treat, prevent, or ameliorate conditions associated with (type I or type II) diabetes mellitus, including, but not limited to, diabetic ketoacidosis, diabetic coma, nonketotic hyperglycemic-hyperosmolar coma, seizures, mental confusion, drowsiness, cardiovascular disease (e.g.,.
- SUMM [0665] Other disorders and/or diseases of the male reproductive system include, for example, Klinefelter's syndrome, Young's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, high fever, multiple sclerosis, and gynecomastia.
- SUMM . . . abortion, complete abortion, habitual abortion, missed abortion, and septic abortion; ectopic pregnancy, anemia, Rh incompatibility, vaginal bleeding during pregnancy, gestational diabetes, intrauterine growth retardation, polyhydramnios, HELLP syndrome, abruptio placentae, placenta previa, hyperemesis, preeclampsia, eclampsia, herpes gestationis, and urticaria of pregnancy. Additionally, . . . high blood pressure, anemia, kidney disease, infectious disease (e.g., rubella, cytomegalovirus, toxoplasmosis, infectious hepatitis, chlamydia, HIV, AIDS, and genital herpes), diabetes mellitus, Graves' disease, thyroiditis, hypothyroidism, Hashimoto's thyroiditis, chronic active hepatitis, cirrhosis of the liver, primary biliary cirrhosis, asthma, systemic lupus. .
- DETD . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.
- DETD . . . administered in combination with one or more of the following: a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a sulfonylurea antidiabetic agent.
- DETD . . . fumarate (e.g., FEOSTAT.TM.), ferrous gluconate (e.g., FERGON.TM.), polysaccharide-iron complex (e.g., NIFEREX.TM.), iron dextran injection (e.g., INFED.TM.), cupric sulfate, pyroxidine, riboflavin, Vitamin B.sub.12, cyancobalamin injection (e.g., REDISOL.TM., RUBRAMIN PC.TM.), hydroxocobalamin, folic acid (e.g., FOLVITE.TM.), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or WELLCOVORIN. . .
- AN 2002:99088 USPATFULL
- TI Kringle domain-containing polynucleotides, polypeptides, and antibodies
- IN Ni, Jian, Germantown, MD, UNITED STATES
  Moore, Paul A., Germantown, MD, UNITED STATES
  Ruben, Steven M., Olney, MD, UNITED STATES
- PI US 2002051984 A1 20020502
- AI US 2001-848288 A1 20010504 (9)
- RLI Continuation-in-part of Ser. No. WO 2000-US30664, filed on 8 Nov 2000, UNKNOWN

PRAI US 1999-164853P 19991112 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 22 ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 12041

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

## L2 ANSWER 45 OF 52 USPATFULL

- DETD . . . and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)
- DETD . . . Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.
- DETD . . . characterized by inflammation (e.g., hepatitis, rheumatoid arthritis, gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant rejection).
- DETD . . . are not limited to, infantile genetic agranulocytosis, familial neutropenia, cyclic neutropenia, neutropenias resulting from or associated with dietary deficiencies (e.g., vitamin B 12 deficiency or folic acid deficiency), neutropenias resulting from or associated with drug treatments (e.g., antibiotic regimens such as. .
- DETD . . . autoimmune and chronic inflammatory and infective diseases. Examples of autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.
- DETD . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or. .
- DETD . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type I diabetes mellitus (insulin dependent diabetes mellitus, IDDM).
- DETD . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type II diabetes mellitus (insulin resistant diabetes mellitus).
- DETD . . . antagonistic antibodies) may be used to diagnose, prognose, treat, prevent, and/or ameliorate conditions associated with (type I or type II) diabetes mellitus, including, but not limited to, diabetic ketoacidosis, diabetic coma, nonketotic hyperglycemic-hyperosmolar coma, seizures, mental confusion, drowsiness, cardiovascular disease (e.g.,. . .
- DETD . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates

```
such as vanadyl sulfate mono- and trihydrates.
DETD
       . . mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of
       Thiamine HCL; 0.365 mg/L of Thymidine; 0.680 mg/L of Vitamin
       B.sub.12; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine; 0.105
       mg/L of Lipoic Acid; 0.081 mg/L of Sodium.
DETD
            . administered in combination with one or more of the following:
       a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a
       sulfonylurea antidiabetic agent.
DETD
       [1366] The diabetic animals have many of the characteristic features
       observed in Type II diabetes mellitus. Homozygous (db+/db+)
       mice are obese in comparison to their normal heterozygous (db+/+m)
       littermates. Mutant diabetic (db+/db+) mice have a. . . glomerular
       filtration abnormalities have been described in these animals (Norido,
       F. et al., Exp. Neurol. 83(2):221-232 (1984); Robertson et al.,
       Diabetes 29(1):60-67 (1980); Giacomelli et Lab Invest.
       40(4):460-473 (1979); Coleman, D. L., Diabetes 31 (Suppl):1-6
       (1982)). These homozygous diabetic mice develop hyperglycemia that is
       resistant to insulin analogous to human type II diabetes
       (Mandel et al., J. Immunol. 120:1375-1377 (1978)).
DETD
            . characteristics observed in these animals suggests that healing
       in this model may be similar to the healing observed in human
       diabetes (Greenhalgh, et al., Am. J. of Pathol. 136:1235-1246
       (1990)).
DETD
                (CCR5) is administered to db+/db+ mice parenterally for various
      periods of time either before or after the mice have developed
      diabetes, and blood glucose, and/or insulin levels, or other
       art-known methods for measuring disease severity, are measured to
       determine whether administration prevents, slows, or lessens the onset
       or severity of diabetes.
       2002:92268 USPATFULL
AN
TΤ
       Human G-protein Chemokine Receptor HDGNR10
       Rosen, Craig A., Laytonsville, MD, UNITED STATES
IN
       Roschke, Viktor, Rockville, MD, UNITED STATES
       Li, Yi, Sunnyvale, CA, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002048786
                          Α1
                               20020425
ΑI
      US 2001-779879
                          A1
                               20010209 (9)
PRAI
      US 2000-181258P
                           20000209 (60)
      US 2000-187999P
                           20000309 (60)
                           20000922 (60)
      US 2000-234336P
      Utility
DT
FS
      APPLICATION
       STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE
LREP
       600, WASHINGTON, DC, 20005-3934
CLMN
      Number of Claims: 61
ECL
       Exemplary Claim: 1
DRWN
       4 Drawing Page(s)
LN.CNT 17969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 46 OF 52 USPATFULL
L2
      Metforimin-containing compositions for the treatment of diabetes
TI
       Compositions and methods using same for the treatment of
AΒ
       diabetes its sequelae and pre-diabetic conditions are provided.
       Invention compositions include the anti-diabetic agent metformin, and
      bioavailable sources of one or.
SUMM
               conditions. Particularly, this invention relates to
      metformin-containing pharmaceutical compositions and to methods of using
       the same for the treatment of diabetes and a number of
       symptoms which precede and/or accompany diabetes.
```

Diabetes mellitus is a mammalian condition in which the amount

of glucose in the blood plasma is abnormally high. Elevated glucose.

SUMM

condition can be life-threatening and high glucose levels in the blood plasma (hyperglycemia) can lead to a number of chronic diabetes syndromes, for example, atherosclerosis, microangiopathy, kidney disorders or failure, cardiac disease, diabetic retinopathy and other ocular disorders, including blindness. SUMM Diabetes mellitus is known to affect at least 10 million Americans, and millions more may unknowingly have the disease. There are two forms of the disease. In the form of this disease known as Type II, non-insulin dependent diabetes (NIDDM) or adult-onset (as opposed to juvenile diabetes or Type I), the pancreas often continues to secrete normal amounts of insulin. However, this insulin is ineffective in preventing the symptoms of diabetes which include cardiovascular risk factors such as hyperglycemia, impaired carbohydrate (particularly glucose) metabolism, glycosuria, decreased insulin sensitivity, centralized obesity hypertriglyceridemia,. various cardiovascular effects attending these risk factors. Many of these cardiovascular risk factors are known to precede the onset of diabetes by as much as a decade. These symptoms, if left untreated, often lead to severe complications, including premature atherosclerosis, retinopathy,. SUMM Current drugs used for managing Type II diabetes and its precursor syndromes, such as insulin resistance, fall within five classes of compounds: the biguanides, thiazolidinediones, the sulfonylureas, benzoic acid derivatives and .alpha.-glucosidase inhibitors. The biguanides, e.g., metformin, are believed to prevent excessive hepatic gluconeogenesis. The thiazolidinediones are believed to act by increasing the rate of peripheral glucose disposal. The sulfonylureas, e.g., tolbutamide and glyburide, the benzoic acid derivatives, e.g. repaglinide, and the .alpha.-glucosidase inhibitors, e.g. acarbose, lower plasma glucose primarily. SUMM

SUMM Unlike sulfonylureas, metformin does not produce hypoglycemia in either diabetic or non-diabetic subjects. With metformin therapy, insulin secretion remains unchanged while fasting. . .

SUMM Currently, there is no composition for the treatment of diabetes, its precursor syndromes and related sequelae that combines metformin with bioavailable elemental nutritional supplements such as vanadium, magnesium and chromium as well as other non-elemental nutritional palliatives which are effective in managing diabetes, its precursors, and sequelae.

SUMM . . . more nutritional supplements in an amount sufficient to produce a desirable effect, such as bioavailable sources of vanadium, chromium, magnesium, vitamin E, lipoic acid, folate and the like.

Additionally, compositions of the present invention may contain aspirin. The present invention improves upon current regimens for treating diabetes with metformin, by exploiting the insulin-like effects of vanadium and chromium and also by providing a source of magnesium, which is so often deficient in people with diabetes. Also provided are methods for the treatment of diabetes and conditions attending or commonly preceding diabetes, comprising administration of an effective amount of the aforementioned compositions.

SUMM . . . to the aforementioned components, an effective amount of one or more additional anti-diabetic agents such as insulin, a thiazolidinedione, a sulfonylurea, a benzoic acid derivative, an .alpha.-glucosidase inhibitor, exendin-4, or the like. As will be apprecitated by those skilled in the. . .

SUMM . . . in the practice of the present invention. Generally, a fixed dosage regimen is individualized for the management of hyperglycemia in diabetes mellitus with metformin HCl or any other pharmacologic agent. Individualization of dosage is made on the basis of both effectiveness. . .

SUMM As readily recognized by those of skill in the art, a variety of

sulfonylureas are useful for the treatment of diabetes
. Exemplary sulfonylureas contemplated for use in the practice
of the present invention (with typical daily dosages indicated in
parentheses) include acetohexamide (in. . .

SUMM . . . readily recognized by those of skill in the art, a variety of alpha-glucosidase inhibitors are useful for the treatment of diabetes. Exemplary alpha-glucosidase inhibitors contemplated for use in the practice of the present invention include acarbose, miglitol, and the like. Effective. . .

SUMM . . . recognized by those of skill in the art, a variety of benzoic acid derivatives are useful for the treatment of **diabetes**.

Exemplary benzoic acid derivatives contemplated for use in the practice of the present invention include repaglinide (effective daily dosage in.

SUMM . . . forms of nutritional supplements such as chromium, vanadium, and magnesium are able to alleviate one or more symptomologies associated with diabetes or which indicate a predisposition to diabetes. As will be understood by those skilled in the art, "bioavailable," as used herein, conotes that a particular element or.

Bioavailable sources of vanadium, such as vanadyl sulfate, and of chromium, such as chromium picolinate, have properties that closely mimic, as well as enhance, many of the physiological. . . cells to insulin, and lowers blood lipid and cholesterol levels. By their ability to potentiate the effects of insulin, both vanadyl sulfate and chromium have been found to enhance the entry of glucose (for energy) and amino acids (for protein synthesis) into. . .

SUMM . . . used to alleviate diabetic and pre-diabetic symptomology, with the vanadyl form being better tolerated physiologically. Bioavailable sources of vanadium include vanadyl sulfate, as well as other bioavailable forms of vanadium known in the art or developed in the future, particularly forms of. . . thus forming a membrane permeable complex that is more permeable than vanadium alone. In one embodiment of the present invention, vanadyl sulfate is present in the range of about 50 mg up to about 7500 mg, per daily dose. In another embodiment of the present invention, vanadyl sulfate is present in the range of about 75 mg up to about 5000 mg, per daily dose. In another embodiment of the present invention, vanadyl sulfate is present in the range of about 20 mg up to about 100 mg, per daily dose.

SUMM . . . of the present invention further optionally comprises, one or more of aspirin or willow bark extracts, a bioavailable source of vitamin E, a bioavailable source of lipoic acid and/or a bioavailable source of folic acid.

Vitamin E improves the action of insulin, glucose metabolism and lipid levels. People with diabetes have been shown to have reduced plasma vitamin E concentrations. As many as 60% of the newly diagnosed diabetic patients also have clinically obvious cardiovascular disease which may be alleviated by the ability of vitamin E to reduce artherosclerosis. Although the exact mechanism by which vitamin E exerts its effects on insulin use is unknown, it is postulated that the effects are the result of the well known antioxidant properties of vitamin E inasmuch as administration of vitamin E has been shown to reduce oxidative stress. Daily oral supplements of vitamin E has been shown to result in strong increase in total glucose disposal and in non-oxidative glucose metabolism in people with diabetes.

SUMM Therefor, in accordance with another aspect of the present invention, vitamin E (free 2R, 4'R, 8'R-alpha tocopherol) may be optionally included in invention compositions in a wide range of concentrations. Any. . . acceptable amount can be employed in the practice of the

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present invention. In one embodiment of the present invention, when vitamin E is included in invention compositions, vitamin E is present in the range of about 100 up to about 800 I.U. per daily dose. In a preferred embodiment, about 400 I.U. of vitamin E is contained per daily dose.
```

SUMM In addition to **vitamin** E, alpha lipoic acid is one of the most powerful antioxidants and is a coenzyme required to breakdown sugars, such. . .

SUMM In accordance with another aspect of the present invention, there are provided methods for the treatment of a subject having **diabetes** mellitus, said method comprising administering to said subject an effective amount of a composition comprising metformin and one or more.

SUMM In accordance with another embodiment of the present invention there are provided methods for the treatment of a subject having diabetes mellitus, said method comprising administering to said subject an effective amount of a composition comprising metformin and one or more.

SUMM As will be appreciated by those of skill in the art, diabetes presents a complicated array of conditions and symptoms including abnormal glucose metabolism, insulin resistance, hyperinsulinemia, hyperglycemia, hypertriglyceridemia, elevated LDL, lowered. . .

SUMM In addition, there are a number of precursor conditions which portend the development of **diabetes** and which can be treated by administration of invention compositions as described herein. Therefor, in accordance with another aspect of. . .

SUMM . . . of the present invention there are provided methods for reducing the doseage of anti-diabetic medication such as a thiazolidinedione, a sulfonylurea, an .alpha.-glucosidase inhibitor or a benzoic acid derivative, said method comprising administering to said subject an effective amount of a. . .

SUMM . . . another aspect of the present invention, there is provided an improvement over methods for the treatment of a subject having diabetes by administering to said subject an effective amount of insulin, the improvement comprising administering to said subject an insulin need. . . .

DETD Effect of Administration of Invention Composition to Patient with

DETD To test the efficacy of invention compositions, a supplement (detailed below) was administered daily to a female with type II diabetes who was experiencing poor blood sugar control while taking metformin 500 mg b.i.d.

DETD

Chromium 333 .mu.g (in the form of 1 mg Cr-picolinate) Magnesium 46 mg (in the form of 384 mg MgCl)

Vanadyl-sulfate hydrate 100 mg

Vitamin E 400 I.U.

Folate 400 .mu.g

DETD Effect of Administration of Invention Composition to Patient with Diabetes

DETD . . . efficacy of invention compositions, a supplement (detailed below) was administered daily to a 27 year old female with type II diabetes who was experiencing poor blood sugar control while taking metformin 1000 mg b.i.d.

DETD

Chromium 333 .mu.g (in the form of 1 mg Cr-picolinate)
Magnesium 46 mg (in the form of 384 mg MgCl)

Vanadyl-sulfate hydrate 100 mg

Vitamin E 400 I.U.
Folate 400 .mu.g

CLM What is claimed is:

- 1. A composition for the treatment of **diabetes**, said composition comprising metformin; one or more of a bioavailable source of magnesium and pharmaceutically acceptable salts thereof; one or. .
- . thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components synergistically treat diabetes.
- 3. A composition according to claim 1, wherein said bioavailable source of vanadium is **vanadyl sulfate**.
- 5. A composition according to claim 1, further comprising one or more of aspirin, a bioavailable source of **vitamin** E, a bioavailable source of .alpha.-lipoic acid or a bioavailable source of folic acid.
- 9. A composition according to claim 3, wherein the amount of **vanadyl sulfate** is in the range of about 20 mg up to about 100 mg, per dose.
- 14. A composition according to claim 5, wherein the amount of **vitamin** E is in the range of about 400 up to about 800 I.U. per dose.
- 19. A composition according to claim 18, wherein said anti-diabetic agent is insulin, a thiazolidinedione, a sulfonylurea, an .alpha.-glucosidase inhibitor or a benzoic acid derivative.
- 20. A composition according to claim 19, wherein said sulfonylurea is acetohexamide, chlorpropamide, tolazimide, tolbutamide, glycazide, glipizide, glyburide, or glimeperide.
- 25. A method for the treatment of **diabetes** mellitus in a subject having **diabetes** mellitus, said method comprising administering to said subject an effective amount of a composition comprising metformin; one or more of. . . thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components synergistically treat **diabetes** mellitus.
- . 36. A method according to claim 35, wherein said anti-diabetic medication is one or more of insulin, a thiazolidinedione, a sulfonylurea, an .alpha.-glucosidase inhibitor or a benzoic acid derivative.
- 38. In a method for the treatment of **diabetes** in a subject having **diabetes** by administering to said subject an effective amount of insulin, the improvement comprising administering to said subject an insulin need. . .
- AN 2002:88529 USPATFULL
- TI Metforimin-containing compositions for the treatment of diabetes
- IN Fine, Stuart A., Northbrook, IL, United States Kinsella, Kevin J., La Jolla, CA, United States
- PA Akesis Pharmaceuticals, Inc., La Jolla, CA, United States (U.S.
- corporation)
- PI US 6376549 B1 20020423
- AI US 1998-156102 19980917 (9)
- DT Utility|
- FS GRANTED!
- EXNAM Primary Examiner: Criares, Theodore J. |
- LREP Foley, Hoag & Eliot LLP|
- CLMN Number of Claims: 40|

ECL Exemplary Claim: 1|
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)|
LN.CNT 1429|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- L2 ANSWER 47 OF 52 USPATFULL
- DETD . . . and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., **Diabetes** 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993)).
- DETD . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or. .
- DETD . . . Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.
- DETD . . . venous stasis ulcers, bums resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. stanniocalcin polynucleotides or polypeptides, . . .
- DETD . . . polynucleotides or polypeptides, as well as agonists or antagonists of stanniocalcin, could be used treat or prevent the onset of diabetes mellitus. In patients with newly diagnosed Types I and II diabetes, where some islet cell function remains, stanniocalcin polynucleotides or polypeptides, as well as agonists or antagonists of stanniocalcin, could be. . .
- DETD . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.
- DETD . . . administered in combination with one or more of the following: a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a sulfonylurea antidiabetic agent.
- DETD . . . fumarate (e.g., FEOSTAT.TM.), ferrous gluconate (e.g., FERGON.TM.), polysaccharide-iron complex (e.g., NIFEREX.TM.), iron dextran injection (e.g., INFED.TM.), cupric sulfate, pyroxidine, riboflavin, Vitamin B.sub.12, cyancobalamin injection (e.g., REDISOL.TM., RUBRAMIN PC.TM.), hydroxocobalamin, folic acid (e.g., FOLVITE.TM.), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or WELLCOVORIN. . .
- AN 2002:78715 USPATFULL
- TI Stanniocalcin polynucleotides, polypeptides, and methods based thereon
- IN Olsen, Henrik S., Gaithersburg, MD, UNITED STATES Zhang, Ke-Zhou, Brussels, BELGIUM Lindsberg, Perttu, Helsinki, FINLAND Tatlisumak, Turgut, Helsinki, FINLAND Kaste, Markku, Vantaa, FINLAND Andersson, Leif C., Helsinki, FINLAND
- PA Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S. corporation)

US 2002042372 PΙ 20020411 A1 ΑI US 2001-840989 A1 20010425 (9) RLI Continuation-in-part of Ser. No. WO 2000-US29432, filed on 26 Oct 2000, UNKNOWN PRAI US 1999-161740P 19991027 (60) DTUtility FS APPLICATION LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850 CLMN Number of Claims: 47 ECL Exemplary Claim: 1 DRWN 12 Drawing Page(s) LN.CNT 9559 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

## L2 ANSWER 48 OF 52 USPATFULL

SUMM . . . and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., **Diabetes** 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993)).

SUMM . . . thrombocytopenia, idiopathic thrombocytopenia purpura, purpura (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease (hyperthyroidism), and insulin-resistant diabetes mellitus.

SUMM . . . polychondritis, rheumatic heart disease, neuritis, uveitis ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome, autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disorders.

SUMM . . . and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone ANA (SS-B)), diabetes mellitus (often characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with. . .

SUMM . . . characterized by inflammation (e.g., hepatitis, rheumatoid arthritis, gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant rejection).

SUMM . . . autoimmune and chronic inflammatory and infective diseases. Examples of autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.

SUMM . . . hypochromic anemia, microcytic anemia, chlorosis, hereditary siderob; astic anemia, idiopathic acquired sideroblastic anemia, red cell aplasia, megaloblastic anemia (e.g., pernicious anemia, (vitamin B12 deficiency) and folic acid deficiency anemia), aplastic anemia, hemolytic anemias (e.g., autoimmune helolytic anemia, microangiopathic hemolytic anemia, and paroxysmal. . .

SUMM . . . are not limited to, infantile genetic agranulocytosis, familial neutropenia, cyclic neutropenia, neutropenias resulting from or associated with dietary deficiencies (e.g., vitamin B 12 deficiency or folic acid deficiency), neutropenias resulting from or associated with drug treatments (e.g., antibiotic regimens such as. .

SUMM . . . treat metabolic and congenital disorders of the kidney (e.g., uremia, renal amyloidosis, renal osteodystrophy, renal tubular acidosis, renal glycosuria, nephrogenic diabetes insipidus, cystinuria, Fanconi's syndrome, renal fibrocystic osteosis (renal rickets), Hartnup disease, Bartter's syndrome, Liddle's syndrome, polycystic kidney disease, medullary cystic disease, medullary sponge kidney, Alport's syndrome, nail-patella syndrome, congenital nephrotic syndrome, CRUSH syndrome, horseshoe kidney, diabetic nephropathy, nephrogenic

diabetes insipidus, analgesic nephropathy, kidney stones, and membranous nephropathy), and autoimmune disorders of the kidney (e.g., systemic lupus erythematosus (SLE), Goodpasture. . .

SUMM . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

- SUMM . . . venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as. . .
- SUMM . . . polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of **diabetes** mellitus. In patients with newly diagnosed Types I and II **diabetes**, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could. . .
- SUMM . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or.
- SUMM [0636] Endocrine system and/or hormone imbalance disorders and/or diseases include disorders and/or diseases of the pancreas, such as, for example, diabetes mellitus, diabetes insipidus, congenital pancreatic agenesis, pheochromocytoma--islet cell tumor syndrome; disorders and/or diseases of the adrenal glands such as, for example, Addison's. . .
- SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type I diabetes mellitus (insulin dependent diabetes mellitus, IDDM).
- SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type II diabetes mellitus (insulin resistant diabetes mellitus).
- SUMM . . . antagonistic antibodies) may be used to diagnose, prognose, treat, prevent, or ameliorate conditions associated with (type I or type II) diabetes mellitus, including, but not limited to, diabetic ketoacidosis, diabetic coma, nonketotic hyperglycemic-hyperosmolar coma, seizures, mental confusion, drowsiness, cardiovascular disease (e.g.,.
- SUMM [0651] Other disorders and/or diseases of the male reproductive system include, for example, Klinefelter's syndrome, Young's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, high fever, multiple sclerosis, and gynecomastia.
- SUMM . . . abortion, complete abortion, habitual abortion, missed abortion, and septic abortion; ectopic pregnancy, anemia, Rh incompatibility, vaginal bleeding during pregnancy, gestational diabetes, intrauterine growth retardation, polyhydramnios, HELLP syndrome, abruptio placentae, placenta previa, hyperemesis, preeclampsia, eclampsia, herpes gestationis, and urticaria of pregnancy. Additionally, . . high blood pressure, anemia, kidney disease, infectious disease (e.g., rubella, cytomegalovirus, toxoplasmosis,

infectious hepatitis, chlamydia, HIV, AIDS, and genital herpes), diabetes mellitus, Graves' disease, thyroiditis, hypothyroidism, Hashimoto's thyroiditis, chronic active hepatitis, cirrhosis of the liver, primary biliary cirrhosis, asthma, systemic lupus. DETD such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates. DETD . 'administered in combination with one or more of the following: a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a sulfonylurea antidiabetic agent. DETD . fumarate (e.g., FEOSTAT.TM.), ferrous gluconate (e.g., FERGON.TM.), polysaccharide-iron complex (e.g., NIFEREX.TM.), iron dextran injection (e.g., INFED.TM.), cupric sulfate, pyroxidine, riboflavin, Vitamin B, .sub.2, cyancobalamin injection (e.g., REDISOL.TM., RUBRAMIN PC.TM.), hydroxocobalamin, folic acid (e.g., FOLVITE.TM.), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or WELLCOVORIN. 2002:66870 USPATFULL IL-6-like polynucleotides, polypeptides, and antibodies Ruben, Steven M., Olney, MD, UNITED STATES Shi, Yanggu, Gaithersburg, MD, UNITED STATES US 2002037523 A1 20020328 20010607 (9) US 2001-875016 Α1 Continuation-in-part of Ser. No. WO 2000-US33134, filed on 7 Dec 2000, UNKNOWN PRAI US 1999-169838P 19991209 (60) Utility APPLICATION LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850 CLMN Number of Claims: 22 Exemplary Claim: 1 No Drawings DRWN LN.CNT 11587 CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 49 OF 52 USPATFULL SUMM . and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993)). thrombocytopenia, idiopathic thrombocytopenia purpura, purpura SUMM (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease (hyperthyroidism), and insulin-resistant diabetes mellitus. SUMM . polychondritis, rheumatic heart disease, neuritis, uveitis ophthalmia, polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome, autoimmune pulmonary inflammation, autism, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disorders. SUMM . and complement in basement membrane), Sjogren's syndrome (often characterized, e.g., by multiple tissue antibodies, and/or a specific nonhistone ANA (SS-B)), diabetes mellitus (often characterized, e.g., by cell-mediated and humoral islet cell antibodies), and adrenergic drug resistance (including adrenergic drug resistance with. SUMM . characterized by inflammation (e.g., hepatitis, rheumatoid arthritis, gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal ischemia-reperfusion injury, Grave's disease, systemic lupus erythematosus, diabetes mellitus, and allogenic transplant

ΑN

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ΑI

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ECL

rejection).

RLI

SUMM . . . autoimmune and chronic inflammatory and infective diseases. Examples of autoimmune diseases are described herein and include multiple sclerosis, and insulin-dependent diabetes.

SUMM . . . hypochromic anemia, microcytic anemia, chlorosis, hereditary siderob; astic anemia, idiopathic acquired sideroblastic anemia, red cell aplasia, megaloblastic anemia (e.g., pernicious anemia, (vitamin B12 deficiency) and folic acid deficiency anemia), aplastic anemia, hemolytic anemias (e.g., autoimmune helolytic anemia, microangiopathic hemolytic anemia, and paroxysmal. . .

SUMM . . . are not limited to, infantile genetic agranulocytosis, familial neutropenia, cyclic neutropenia, neutropenias resulting from or associated with dietary deficiencies (e.g., vitamin B 12 deficiency or folic acid deficiency), neutropenias resulting from or associated with drug treatments (e.g., antibiotic regimens such as. .

SUMM . . . treat metabolic and congenital disorders of the kidney (e.g., uremia, renal amyloidosis, renal osteodystrophy, renal tubular acidosis, renal glycosuria, nephrogenic diabetes insipidus, cystinuria, Fanconi's syndrome, renal fibrocystic osteosis (renal rickets), Hartnup disease, Bartter's syndrome, Liddle's syndrome, polycystic kidney disease, medullary cystic disease, medullary sponge kidney, Alport's syndrome, nail-patella syndrome, congenital nephrotic syndrome, CRUSH syndrome, horseshoe kidney, diabetic nephropathy, nephrogenic diabetes insipidus, analgesic nephropathy, kidney stones, and membranous nephropathy), and autoimmune disorders of the kidney (e.g., systemic lupus erythematósus (SLE), Goodpasture. . .

SUMM . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

SUMM . . . venous stasis ulcers, burns resulting from heat exposure or chemicals, and other abnormal wound healing conditions such as uremia, malnutrition, vitamin deficiencies and complications associated with systemic treatment with steroids, radiation therapy and antineoplastic drugs and antimetabolites. Polynucleotides or polypeptides, as. . .

SUMM . . . polypeptides, as well as agonists or antagonists of the present invention, could be used treat or prevent the onset of **diabetes** mellitus. In patients with newly diagnosed Types I and II **diabetes**, where some islet cell function remains, polynucleotides or polypeptides, as well as agonists or antagonists of the present invention, could. . .

SUMM . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or. .

SUMM [0654] Endocrine system and/or hormone imbalance disorders and/or diseases include disorders and/or diseases of the pancreas, such as, for example, diabetes mellitus, diabetes insipidus, congenital pancreatic agenesis, pheochromocytoma—islet cell tumor syndrome; disorders and/or diseases of the adrenal glands such as, for example, Addison's. . .

SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type I diabetes mellitus (insulin dependent diabetes

mellitus, IDDM). SUMM ' . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type II diabetes mellitus (insulin resistant diabetes mellitus). SUMM . . . antagonistic antibodies) may be used to diagnose, prognose, treat, prevent, or ameliorate conditions associated with (type I or type II) diabetes mellitus, including, but not limited to, diabetic ketoacidosis, diabetic coma, nonketotic hyperglycemic-hyperosmolar coma, seizures, mental confusion, drowsiness, cardiovascular disease (e.g.,. [0669] Other disorders and/or diseases of the male reproductive system SUMM include, for example, Klinefelter's syndrome, Young's syndrome, premature ejaculation, diabetes mellitus, cystic fibrosis, Kartagener's syndrome, high fever, multiple sclerosis, and gynecomastia. SUMM . . . abortion, complete abortion, habitual abortion, missed abortion, and septic abortion; ectopic pregnancy, anemia, Rh incompatibility, vaginal bleeding during pregnancy, gestational diabetes, intrauterine growth retardation, polyhydramnios, HELLP syndrome, abruptio placentae, placenta previa, hyperemesis, preeclampsia, eclampsia, herpes gestationis, and urticaria of pregnancy. Additionally,. . . high blood pressure, anemia, kidney disease, infectious disease (e.g., rubella, cytomegalovirus, toxoplasmosis, infectious hepatitis, chlamydia, HIV, AIDS, and genital herpes), diabetes mellitus, Graves' disease, thyroiditis, hypothyroidism, Hashimoto's thyroiditis, chronic active hepatitis, cirrhosis of the liver, primary biliary cirrhosis, asthma, systemic lupus. . . . . such as, for example, ammonium metavanadate, sodium DETD metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates. DETD administered in combination with one or more of the following: a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a

sulfonylurea antidiabetic agent.

DETD fumarate (e.g., FEOSTAT.TM.), ferrous gluconate (e.g., FERGON.TM.), polysaccharide-iron complex (e.g., NIFEREXT.TM.), iron dextran injection (e.g., INFED.TM.), cupric sulfate, pyroxidine, riboflavin, Vitamin B.sub.12, cyancobalamin injection (e.g., REDISOL.TM., RUBRAMIN PC.TM.), hydroxocobalamin, folic acid (e.g., FOLVITE.TM.), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or WELLCOVORIN.

2002:12261 USPATFULL AN

Uteroglobin-like polynucleotides, polypeptides, and antibodies ΤI

Ni, Jian, Germantown, MD, UNITED STATES IN Ruben, Steven M., Olney, MD, UNITED STATES

A1 20020117 PΙ US 2002006640

ΑI US 2001-846258 A1 20010502 (9)

Continuation-in-part of Ser. No. WO 2000-US30326, filed on 3 Nov 2000, RLI UNKNOWN

US 1999-163395P PRAI 19991104 (60)

DTUtility

FS APPLICATION

HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850 LREP

CLMN Number of Claims: 22

Exemplary Claim: 1 ECL

No Drawings

LN.CNT 12076

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 50 OF 52 USPATFULL

[0003] Natural retinoids regulate the growth and differentiation of a SUMM

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wide variety of cell types, and include Vitamin A and its
       biologically active derivatives retinal and retinoic acid. Retinoids act
       as morphogenic agents during embryonic development, and play.
SUMM
         . . nuclear hormone receptors by retinoid binding, these receptors
       undergo homodimerization or heterodimerization with other family
       members, including thyroid hormone receptor, vitamin D
       receptor, and retinoid X receptor interacting proteins (RIPs), such as
       RIP14 and RIP15 (Seol, W., et al, (1995)). These.
       . . and increases clearance due to the aggregate's immunogenic
SUMM
       activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967);
       Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al.,
       Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993)).
SUMM
       . . . thrombocytopenia, idiopathic thrombocytopenia purpura, purpura
       (e.g., Henloch-Scoenlein purpura), autoimmunocytopenia, Goodpasture's
       syndrome, Pemphigus vulgaris, myasthenia gravis, Grave's disease
       (hyperthyroidism), and insulin-resistant diabetes mellitus.
SUMM
       . . . polychondritis, rheumatic heart disease, Neuritis, Uveitis
       Ophthalmia, Polyendocrinopathies, Reiter's Disease, Stiff-Man Syndrome,
       Autoimmune Pulmonary Inflammation, Autism, Guillain-Barre Syndrome,
       insulin dependent diabetes mellitis, and autoimmune
       inflammatory eye.
       . . . and complement in basement membrane), Sjogren's syndrome (often
SUMM
       characterized, e.g., by multiple tissue antibodies, and/or a specific
       nonhistone ANA (SS-B)), diabetes millitus (often
       characterized, e.g., by cell-mediated and humoral islet cell
       antibodies), and adrenergic drug resistance (including adrenergic drug
       resistance with.
SUMM
            . inflammation (such as, e.g., hepatitis, rheumatoid arthritis,
       gout, trauma, pancreatitis, sarcoidosis, dermatitis, renal
       ischemia-reperfusion injury, Grave's disease, systemic lupus
       erythematosis, diabetes mellitus, and allogenic transplant
       rejection).
SUMM
       . . . autoimmune and chronic inflammatory and infective diseases.
       Examples of autoimmune diseases are described herein and include
      multiple sclerosis, and insulin-dependent diabetes.
SUMM
         . . such as, for example, ammonium metavanadate, sodium
      metavanadate, and sodium orthovanadate. Suitable vanadyl complexes
       include, for example, vanadyl acetylacetonate and vanadyl
       sulfate including vanadyl sulfate hydrates
       such as vanadyl sulfate mono- and trihydrates.
SUMM
            . venous stasis ulcers, burns resulting from heat exposure or
       chemicals, and other abnormal wound healing conditions such as uremia,
       malnutrition, vitamin deficiencies and complications associted
       with systemic treatment with steroids, radiation therapy and
       antineoplastic drugs and antimetabolites. Polynucleotides or
      polypeptides, as.
SUMM
           . polypeptides, as well as agonists or antagonists of the present
       invention, could be used treat or prevent the onset of diabetes
      mellitus. In patients with newly diagnosed Types I and II
       diabetes, where some islet cell function remains,
       polynucleotides or polypeptides, as well as agonists or antagonists of
       the present invention, could.
SUMM
       [0597] Endocrine system and/or hormone imbalance disorders and/or
       diseases include disorders and/or diseases of the pancreas, such as, for
       example, diabetes mellitus, diabetes insipidus,
       congenital pancreatic agenesis, pheochromocytoma--islet cell tumor
       syndrome; disorders and/or diseases of the adrenal glands such as, for
       example, Addison's.
SUMM
       . . . to this gene and/or agonists and/or antagonists thereof may be
       used to diagnose, prognose, treat, prevent, and/or ameliorate type I
```

diabetes mellitus (insulin dependent diabetes

mellitus, IDDM).

SUMM . . . to this gene and/or agonists and/or antagonists thereof may be used to diagnose, prognose, treat, prevent, and/or ameliorate type II diabetes mellitus (insulin resistant diabetes mellitus).

SUMM . . . antagonistic antibodies) may be used to diagnose, prognose, treat, prevent, or ameliorate conditions associated with (type I or type II) diabetes mellitus, including, but not limited to, diabetic ketoacidosis, diabetic coma, nonketotic hyperglycemic-hyperosmolar coma, seizures, mental confusion, drowsiness, cardiovascular disease (e.g.,.

SUMM . . . the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including, but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration; (7) neurological lesions associated with systemic diseases including, but not limited to, diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis; (8) lesions caused by toxic substances including alcohol, lead, or.

DETD . . . such as, for example, ammonium metavanadate, sodium metavanadate, and sodium orthovanadate. Suitable vanadyl complexes include, for example, vanadyl acetylacetonate and vanadyl sulfate including vanadyl sulfate hydrates such as vanadyl sulfate mono- and trihydrates.

DETD . . . administered in combination with one or more of the following: a biguanide antidiabetic agent, a glitazone antidiabetic agent, and a sulfonylurea antidiabetic agent.

DETD . . . fumarate (e.g., FEOSTAT.TM.), ferrous gluconate (e.g., FERGON.TM.), polysaccharide-iron complex (e.g., NIFEREX.TM.), iron dextran injection (e.g., INFED.TM.), cupric sulfate, pyroxidine, riboflavin, Vitamin B.sub.12, cyancobalamin injection (e.g., REDISOL.TM., RUBRAMIN PC.TM.), hydroxocobalamin, folic acid (e.g., FOLVITE.TM.), leucovorin (folinic acid, 5-CHOH4PteGlu, citrovorum factor) or WELLCOVORIN. . .

AN 2002:8489 USPATFULL

TI Retinoid receptor interacting polynucleotides, polypeptides, and antibodies

IN Shi, Yanggu, Gaithersburg, MD, UNITED STATES Ruben, Steven M., Olney, MD, UNITED STATES

PI US 2002004489 A1 20020110

AI US 2001-788600 A1 20010221 (9)

RLI Continuation-in-part of Ser. No. WO 2000-US22351, filed on 15 Aug 2000, UNKNOWN

PRAI US 1999-148757P 19990816 (60) US 2000-189026P 20000314 (60)

DT Utility

FS APPLICATION

LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 11257

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 51 OF 52 USPATFULL

AB A daily nutritional supplement and method of administering it to assist in the metabolism of glucose for patients with diabetes and pre-diabetes is disclosed. The supplement preferably includes anchor components of Chromium Polynicotinate and Picolinate, Vanadyl Sulfate, Vitamin E Natural, Standardized Willow Bark (aspirin), and Magnesium Chloride, Citrate,

Fumarate, Malate, Glutorate, and Succinate Complex, Folic Acid, and Alpha-Lipoic. SUMM The present invention is related to a unique vitamin, mineral, and herbal supplement for the treatment of both type I and II diabetes, and for the prevention of type II diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT). Specifically, the present invention is directed towards a dietary supplement for diabetic control containing a plurality of compounds from the following group: Vanadyl sulfate, Chromium polynicotinate and picolinate, Magnesium chloride, citrate, fumarate, malate, glutorate, and succinate complex, Natural Vitamin E (free 2R, 4'R, 8'R-alpha tocopherol), Standardized Willow Bark (aspirin), Alpha-lipoic acid, and Folic acid. SUMM Diabetes has become a leading health care issue in the United States and other industrialized countries, accounting for one seventh of the entire national health care product. The incidence of diagnosed diabetes has increased five-fold in America over the past 35 years, with currently 8 million diagnosed diabetic patients, another estimated 8 to 12 million undiagnosed diabetic individuals, and still an additional 23 million Americans with pre-diabetes, or impaired glucose tolerance (IGT). As the American populace continues its strong trend towards aging, obesity and greater minority representation, the increasing rate of diagnosed diabetes is certain to continue. SUMM The tremendous economic and physical toll diabetes extracts from society is, in large part, secondary to both the short and long-term complications of the disease. While there have been great strides made in reducing the short term complications of diabetes, e.g. ketoacidosis, dehydration, and non-ketotic hyperosmolar coma, little, if any, headway has been made in preventing or even minimizing the devastating chronic complications of the disease, e.g. premature atherosclerosis, retinopathy, nephropathy, and neuropathy. Indeed, diabetes has become the leading cause of new cases of blindness in adults in the United States, and now accounts SUMM Diabetes is a major cardiovascular risk factor, especially among women. This increased risk factor in women is a fact lost by. in both the medical and lay communities. Indeed, a man's risk of dying by heart disease doubles when he develops diabetes, but a woman's risk increases three to five-fold the day she is found to have diabetes. The failure to reduce this increased risk for heart disease over the last eight decades of diabetes management is a painful reminder that our current interventions, while having the potential for more favorable impact, are woefully inadequate. SUMM Type II diabetes [(i.e. maturity onset)], which accounts for 95% of diabetes, is far more than just a state of abnormal glucose metabolism, but is rather a milieu of co-existent cardiovascular metabolic. . . elevated blood pressure: a state recently identified as Syndrome X. Much of the excessive cardiovascular morbidity and mortality associated with diabetes is secondary to this array of cardiovascular risk factors, which precede the onset of diabetes by as much as a decade and may explain the presence of overt clinical cardiovascular disease in as many as. SUMM . such as hypertension, dyslipidemia and cigarette smoking. The inventor of the present invention has popularized the term "dead zone of diabetes" to describe this phenomenon of increased cardiovascular risk even after allowing for the co-existence of other risk factors in diabetes. This `dead zone" is secondary to both the atherogenicity of insulin resistance, which precedes the onset of diabetes by at least 8 years, and the atherogenicity of undiagnosed and uncontrolled hyperglycemia, which is present for 9-12 years before diabetes is first diagnosed. Treatment of

diabetes, and its related chronic symptoms and risk factors, are

best treated at this early stage.

SUMM If the medical community is to have any success in attenuating the cardiovascular ravages of diabetes, it must stress interventions that reduce insulin resistance, an integral part of type II diabetes, and aggressively control blood glucose, through earlier diagnosis and improved management of diabetes. That is precisely why exercise and dietary modification will always be the mainstay of diabetic management, because both will improve insulin sensitivity and glucose control. Until recently the only available pharmacologic (sulfonylureas and insulin) interventions in this country for diabetes, poorly controlled with exercise and diet, did not address insulin resistance and were inappropriate for use in early type II diabetes. Not surprisingly, their use has failed to reduce the excessive car vascular morbidity of diabetes, and, indeed, may even be associated with increased risk of cardiovascular disease.

SUMM . to reduce insulin resistance, i.e. insulin sensitizers or enhancers, which hopefully may impact more favorably on the cardiovascular complications of diabetes. Unfortunately, these drugs require a prescription and their use in diabetes is markedly delayed, which will likely blunt their efficacy in reducing cardiovascular risk. Indeed, troglitazone was initially indicated in type II diabetes only in combination with insulin, precluding its use in early diabetes.

SUMM . . . developing in these high risk patients. There is also a need to provide an effective supplement for the treatment of diabetes and its symptoms prior to the onset of full-blown diabetes. SUMM The present invention focuses upon a new and unique dietary supplement

specifically formulated for people with diabetes and prediabetes (IGT). This formulation is based upon well-designed, randomized, placebo-controlled double-blind human studies, using specific minerals and trace minerals, antioxidant vitamins. improve blood glucose control, insulin sensitivity, lipid abnormalities, blood pressure, and reduce the risk of heart disease in people with diabetes.

SUMM . . . a source of chromium, an effective amount of a source of vanadium, an effective amount of a source of magnesium, vitamin E and aspirin, and an effective amount of folic acid and alpha-lipoic acid.

SUMM . preferred supplement includes an effective amount of chromium polynicotinate and chromium picolinate as the chromium source, an effective amount of vanadyl sulfate as the vanadium source, an effective amount of magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex as the magnesium source, an effective amount of free 2R, 4'R, 8'R-alpha tocopherol as the natural Vitamin E source, an effective amount of standardized willow bark as the source of aspirin, an effective amount of folic acid and alpha-lipoic acid, as well as sufficient amounts of vitamin and mineral supplements.

SUMM . about 200 mcg and about 1500 mg chromium picolinate and/or chromium polynicotinate, between about 10 mg and about 100 mg vanadyl sulfate, and between about 300 mg and about 400 mg magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex, between about. . . about 30 days. The most preferred daily nutritional supplement contains about 1000 mcg chromium polynicotinate and/or picolinate, about 100 mg vanadyl sulfate, about 384 mg magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex, about 400 I.U. free 2R, 4'.F, 8'R-alpha tocopherol,.

The present invention is related to a unique vitamin, mineral, and herbal supplement for the treatment of both type I and II diabetes, and for the prevention of type II diabetes

SUMM

in those individuals with pre-diabetes, or impaired glucose tolerance (IGT). Specifically, the present invention is directed towards a dietary supplement for diabetic control containing a plurality of compounds from the following group: Vanadyl sulfate, Chromium polynicotinate and picolinate, Magnesium chloride, citrate, fumarate, malate, glutorate, and succinate complex, Natural Vitamin E (free 2R, 4'R, 8'R-alpha tocopherol), Standardized Willow Bark (aspirin), Alpha-lipoic acid, and Folic acid.

- SUMM . . . daily administration of the nutritional supplement. The daily doses of the anchor or key components listed above, in combination with vitamin and mineral supplements, can be used in patients to prevent the development of full blown diabetes or, where the person has diabetes, to reduce the amount of insulin required to control blood glucose levels.
- DETD . . . provides a dietary supplement that enhances glucose metabolism, while treating many of the secondary or risk factors that often accompany diabetes or IGT. While the supplement may be used by individuals with no apparent symptoms of diabetes, the supplement is ideal for use by individuals with IGT and diabetes to prevent, reduce or eliminate the necessity of using insulin or other anti-diabetic medications. However, the supplement contains ingredients which. . .
- Nutritional supplements according to the present invention arc not DETD intended to supplant other forms of diabetes and IGT treatment, such as the appropriate diet and exercise, nor does necessarily it eliminate the need for insulin. Rather,. . . has been discovered that a dietary supplement containing effective amounts of metabolically available forms of vanadium, chromium, magnesium, and natural vitamin E in combination with naturally available sources of aspirin, alpha lipoic acid, and folic acid will improve the metabolism of glucose and arrest or treat many of the cardiovascular complications or risk factors associated with diabetes or prediabetes. These components perform different functions which, when administered in appropriate dosages and forms, enhance the metabolism of glucose. . . itself, while at the same time prevent or reduce the likelihood of a cardiovascular event due to complications associated with diabetes. The importance of each of these key or "anchor" components is set forth below:
- DETD . . . and building muscle mass, are scientifically unfounded, especially in its use for non diabetic individuals. Indeed, chromium supplementation, even in diabetes, is unsettled with the American Diabetes Association's Position Statement declaring, "The only known circumstance in which chromium replacement has any beneficial effect on glycemic, control is. . .
- DETD . . . for chromium supplementation in those individuals who are obviously chromium deficient, the actual prevalence of chromium deficiency in people with diabetes has never been, nor could it be, established. Nonetheless, chromium deficiency is common in diabetic patients, who have lower plasma. . .
- DETD Vanadyl Sulfate (preferred dosage range 10.00-100.00 mg.; most preferred embodiment is 100.00 mg)
- DETD . . . human tissue, has a well documented insulin enhancing effect in laboratory animals. After extensive studies using vanadate in diabetic rats, vanadyl sulfate 100 mg daily was found to significantly improve both hepatic and peripheral insulin sensitivity in patients with type II diabetes. Vanadyl sulfate was the preparation of vanadium chosen because it was not associated with any apparent toxicity during treatment periods of up.
- DETD In a recently published study of moderately obese, insulin resistant type II diabetic patients, treatment with oral **vanadyl** sulfate 100 mg daily for three weeks resulted in a significant

drop in fasting blood glucose levels and a highly significant. . . of cholesterol and a decline, though not statistically significant, in serum triglycerides. Using the hyperinsulinemic-euglycemic clamp, it was shown that vanadyl sulfate dramatically enhanced insulin mediated glucose disposal with an 82% increase in glucose infusion rate. There was also significant reduction in hepatic glucose production, likely secondary to a potentiation of insulin's inhibitory effect on lipolysis by vanadyl sulfate. As in the previous studies, vanadyl sulfate was well tolerated.

- DETD Magnesium, rather, magnesium deficiency, has long been known to be associated with diabetes, both type I and type II. Unlike some of the uncertainties regarding the incidence of chromium deficiency in diabetes, much more is known about the epidemiology and diagnosis of magnesium deficiency in diabetes, though discord regarding the actual prevalence of magnesium deficiency abounds. Indeed, magnesium deficiency may be the most underappreciated and underdiagnosed. . .
- DETD . . . been linked to the Reaven-Modan syndrome and underlies the well-known association of magnesium deficiency to essential hypertension, insulin resistance, hyperinsulinemia, diabetes, congestive heart failure and ischemic heart disease. Also, magnesium deficiency has been associated with an increase in platelet reactivity, a condition known to exist in patients with diabetes, and may help explain the accelerated atherosclerosis and increased rate of acute thrombotic events that so tragically define diabetes. Finally, hypomagnesemia has been implicated in the retinopathic microvascular complication of diabetes, with lower levels of magnesium predicting a greater risk of severe diabetic retinopathy.
- While it is universally accepted that magnesium deficiency is common in both type I and type II diabetes, it is unclear as to the precise incidence of this condition in diabetes. The diabetic patient is certainly at risk for developing magnesium depletion via inadequate dietary intake and gastrointestinal and renal losses, . . . very specific, assessment of magnesium depletion in the body. Even with this exceedingly insensitive measure for magnesium deficiency, patients with diabetes have a 25% to 38% prevalence of hypomagnesemia. Using much more sensitive research-oriented tests (nuclear magnetic resonance spectroscopy and magnesium-selective. . .
- DETD Still, the American Diabetes Association's position on screening, diagnosing and intervening for magnesium deficiency in patients with diabetes remains skeptical, as in the case of chromium deficiency. The inventor of the present invention believes this to be the. . .
- DETD . . . Magnesium, as used in the present invention, is thus expected to improve glucose metabolism and to arrest or reduce any diabetes associated secondary risk factors.
- Vitamin E Natural (free 2R, 4'R, 8'R-alpha tocopherol) (preferred range 400.00-800.00 I.U.; most preferred dosage 400 I.U.)
- Vitamin E is the most widely studied of the antioxidant vitamins. The interest in vitamin E as an antioxidant is based on the many demonstrations in humans that giving vitamin E as a supplement decreases the oxidation of low density lipoprotein (LDL) ex vivo, an event critical in the atherogenic. . .
- Vitamin E supplementation has been shown to significantly reduce experimentally induced atherosclerosis in primates and more recent epidemiological and interventional human studies appear to support this observation. This assumes greater importance in those with diabetes, in view of the fact that as many as 60% of newly diagnosed diabetic patients already have clinically obvious cardiovascular. . .
- DETD . . . disease was observed in a four year, prospective, observational

study in healthy middle-aged men who had higher intakes of dietary vitamin E as compared to those consuming small amounts.

DETD . . . at baseline were found to have a highly significant reduced risk of coronary artery disease if they had been on **vitamin** E supplements for at least two years during the eight year study. In a more recent and similar seven year prospective study of postmenopausal women without cardiovascular disease, dietary **vitamin** E consumption, but not **vitamin** A or C, was inversely associated with the risk of death from coronary artery disease.

Perhaps the most powerful argument for vitamin E supplementation, at least, in those patients with already proven coronary artery disease, is the recently published Cambridge Heart Antioxidant. . . The CHAOS was a nearly three year prospective, secondary interventional trial of 2002 men and women, 10% of whom had diabetes, using natural vitamin E (free 2R, 4'R, 8'R-alpha tocopherol), 400 or 800 I.U. daily, in a randomized, placebo-controlled, double-blinded design. Either dose of vitamin E was associated with a dramatic and significant 77% risk reduction of non-fatal myocardial infarct. The benefit of treatment with vitamin E was apparent after 200 days, and the patients with diabetes also enjoyed the marked reduction in the risk of non-fatal heart disease.

DETD Another unrelated benefit of vitamin E supplementation is the favorable effect it has on insulin sensitivity, glucose metabolism and lipid levels in both healthy subjects and patients with type II diabetes. Conversely, in a prospective study of almost one thousand non diabetic, middle-aged men, low concentration of plasma vitamin E at baseline was found to be an independent and powerful predictor for the development of type II diabetes during the four year study. Remarkably, a low level of vitamin E was associated with a greater than five-fold risk of developing diabetes in the ensuing four years!

Vitamin E was well tolerated in the studies where it was given as a supplement, and in the CHAOS study there. . . effects. Because of the unusually high incidence of clinical heart disease in newly diagnosed diabetic patients, and the favorable effect vitamin E has on the metabolic abnormalities of type II diabetes, the present invention will contain preferably 400-800 I.U.; and most preferably natural vitamin E (free 2R, 4'R, 8'R-alpha tocopherol) 400 I.U.

DETD . . . costs alone would be reduced by \$3 billion per year in this country if the 15 million adults, many with diabetes, who qualify for hypolipidernic medication per NCEP guidelines were to first be given aspirin prophylaxis.

DETD . . . enzyme necessary for the synthesis of thromboxane, a potent stimulator of platelet aggregation, a condition known to be increased in diabetes and to be causative in the atherosclerotic process. In patients with diabetes, aspirin has been shown to correct this abnormal increase in platelet activity.

DETD The cardiovascular protective effect of aspirin in men and women with diabetes was demonstrated in the Early Treatment Diabetic Retinopathy Study. Both type I and II patients were randomized to double-blinded placebo. . .

DETD . . . of alpha-lipoic acid to diabetic patients with neuropathy significantly reduces symptoms. Diabetic neuropathy has been an unusually refractive complication of **diabetes**.

DETD These anchor compounds are most preferably combined with other vitamin and mineral supplements. These additional ingredients are preferably included with the anchor compounds, and should be taken simultaneously.

DETD . . . that sufficient amounts of the most important minerals and vitamins are available, it is preferred that the supplement also include

```
vitamin A (or beta carotene), vitamin C, calcium,
       copper, selenium, and zinc.
DETD
       One example of the preferred embodiment, the "Pro Health Pak," is
       distributed by Diabetes Pro Health of Pittsburgh, Pa. Pro
       Health Pak consists of two major "components." The first, the so-called
       backbone of the.
DETD
        3 tablets Containing Chromium Picolinate and Polynicotinate,
       Vanadyl
          Sulfate, Vitamin E Natural, Standardized Willow
       Bark (aspirin),
        Folic Acid, Alpha-Lipoic Acid and a Multivitamin/Mineral
1 tablet Containing Magnesium Complex consisting of.
        Chromium Polynicotinate and Picolinate 200-1500 mcg.
  Vanadyl Sulfate Hydrate
                                       10-100
  Vitamin E Natural (free 2R, 4'R 8'R-alpha 400-800
tocopherol)
Standardized Willow Bark (aspirin 20-40 mg.) 160-320
Magnesium Chloride, Citrate, II Fumarate, 300-400
Malate, Glutorate and Succinate Complex
                                     400-600
Folic Acid (Folate)
                                               mcg.
Alpha-Lipoic Acid
                                     0-600
                                               mg.
                                       5000 I.U. or 25,000 I.U.
  Vitamin A or Beta Carotene
  Vitamin C
                                       60
                                                 mg.
Thiamine
                                     3.00
                                               mg.
Riboflavin
                                     3.60
                                               mq.
Niacinamide
                                    20.10
                                               mg.
  Vitamin B-6
                                       23.10
                                                 ma.
  Vitamin B-12
                                       48.00
                                                 mcq.
                                    300
Biotin
                                               mcq.
Pantothenic Acid
                                    10.00
                                               mg.
                                    150
Calcium
                                               mg.
                                    115
Phosphorus
                                               mq.
Iodine
                                    150
                                               mcq.
Zinc
                                     15.00
                                               mg.
Selenium
                                     60
                                               mcq.
                                     2.00
Copper
                                               mg.
Manganese.
               containing a 30 day supply. The daily supplement is provided as
DETD
       an individual packet in which 4 tablets are enclosed. Diabetes
       Pro Health provides to the patient with diabetes or
       prediabetes a readily available and affordable and medically proven
       addition to their armamentarium for diabetes management,
      something which has been sorely lacking. Pro Health Pak will be
       recommended for use in patients with diabetes or pre-
       diabetes only as part of a complete diabetes treatment
       or prevention program, and will require regular blood glucose monitoring
       when used in the diabetic patient.
CLM
       What is claimed is:
          chromium comprises one or more of the following: chromium picolinate,
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- and chromium polynicotinate; and said bioavailable source of vanadium comprises vanadyl sulfate.
- 5. The dietary supplement of claim 4, further comprising an effective amount of Vitamin E.
- supplement of claim 1, wherein said bioavailable source of chromium is chromium polynicotinate, and said bioavailable source of vanadium is vanadyl sulfate.
- of said bioavailable source of vanadium has the amount of vanadium in about 10 mg to about 100 mg of vanadyl sulfate.

- 9. The dietary supplement of claim 7, further comprising an effective amount **Vitamin** E.
- . . said amount of said bioavailable source of vanadium has at least the amount of vanadium in about 100 mg of **vanadyl sulfate** 
  - 12. The dietary supplement of claim 11, further comprising an effective amount of **Vitamin** E.
  - 16. The ingestible formulation of claim 13, further comprising an effective amount of one or more of the following: **Vitamin** E, and magnesium.
- . . or more of the following: chromium picolinate, and chromium polynicotinate; and said complex of said bioavailable source of vanadium comprises vanadyl sulfate.
- . . of said bioavailable source of vanadium has the amount of vanadium in about 10 mg to about 100 mg of vanadyl sulfate.
  - 19. The ingestible formulation of claim 18, further comprising an effective amount of one or more of the following: **Vitamin** E, and magnesium.
- . or more of the following: chromium picolinate, and chromium polynicotinate; and said complex of said bioavailable source of vanadium comprises vanadyl sulfate.
- . of said bioavailable source of vanadium delivers the amount of vanadium in about 10 mg to about 100 mg of vanadyl sulfate.
  - . . method of claim 29, wherein said dietary supplement further comprises an effective amount of one or more of the following: **Vitamin** E, and magnesium.
  - . . said complex of said bioavailable source of vanadium delivers at least the amount of vanadium in about 100 mg of **vanady1** sulfate.
- . . method of claim 31, wherein said dietary supplement further comprises an effective amount of one or more of the following: **Vitamin** E, and magnesium.

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AN 2001:40034 USPATFULL
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TI Dietary supplement and method of treatment for diabetic control

IN Fine, Stuart A., Northbrook, IL, United States

PA Akesis Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)

PI US 6203819 B1 20010320 AI US 1999-272819 19990319 (9)

RLI Continuation of Ser. No. US 1997-964814, filed on 5 Nov 1997

PRAI US 1997-39958P 19970307 (60)

DT Utility|

FS Granted

EXNAM Primary Examiner: Jarvis, William R. A.

LREP Foley, Hoag & Eliot | CLMN Number of Claims: 39 | ECL Exemplary Claim: 1 |

DRWN No Drawings

L2 ANSWER 52 OF 52 USPATFULL AΒ A daily nutritional supplement and method of administering it to assist in the metabolism of glucose for patients with diabetes and

pre-diabetes is disclosed. The supplement preferably includes anchor components of Chromium Polynicotinate and Picolinate, Vanadyl Sulfate, Vitamin E Natural, Standardized Willow Bark (aspirin), and Magnesium Chloride, Citrate,

Fumarate, Malate, Glutorate, and Succinate Complex, Folic Acid, and Alpha-Lipoic.

SUMM The present invention is related to a unique vitamin, mineral, and herbal supplement for the treatment of both type I and II diabetes, and for the prevention of type II diabetes in those individuals with pre-diabetes, or impaired glucose tolerance (IGT). Specifically, the present invention is directed towards a dietary supplement for diabetic control containing a plurality of compounds from the following group: Vanadyl sulfate, Chromium polynicotinate and picolinate, Magnesium chloride, citrate, fumarate, malate, glutorate, and succinate complex, Natural Vitamin E (free 2R, 4'R, 8'R-alpha tocopherol), Standardized

Willow Bark (aspirin), Alpha-lipoic acid, and Folic acid. Diabetes has become a leading health care issue in the United

SUMM States and other industrialized countries, accounting for one seventh of the entire national health care product. The incidence of diagnosed diabetes has increased five-fold in America over the past 35 years, with currently 8 million diagnosed diabetic patients, another estimated 8 to 12 million undiagnosed diabetic individuals, and still an additional 23 million Americans with pre-diabetes, or impaired glucose tolerance (IGT). As the American populace continues its strong trend towards aging, obesity and greater minority representation, the increasing rate of diagnosed diabetes is certain to continue.

SUMM The tremendous economic and physical toll diabetes extracts from society is, in large part, secondary to both the short and long-term complications of the disease. While there have been great strides made in reducing the short term complications of diabetes, e.g. ketoacidosis, dehydration, and non-ketotic hyperosmolar coma, little, if any, headway has been made in preventing or even minimizing the devastating chronic complications of the disease, e.g. premature atherosclerosis, retinopathy, nephropathy, and neuropathy. Indeed, diabetes has become the leading cause of new cases of blindness in adults in the United States, and now accounts

Diabetes is a major cardiovascular risk factor, especially SUMM among women. This increased risk factor in women is a fact lost by. in both the medical and lay communities. Indeed, a man's risk of dying by heart disease doubles when he develops diabetes, but a woman's risk increases three to five-fold the day she is found to have diabetes. The failure to reduce this increased risk for heart disease over the last eight decades of diabetes management is a painful reminder that our current interventions, while having the potential for more favorable impact, are woefully inadequate. SUMM Type II diabetes [(i.e. maturity onset)], which accounts for 95% of diabetes, is far more than just a state of abnormal

glucose metabolism, but is rather a milieu of co-existent cardiovascular elevated blood pressure: a state recently identified as Syndrome X. Much of the excessive cardiovascular morbidity and mortality associated with diabetes is secondary to this array of cardiovascular risk factors, which precede the onset of diabetes by as much as a decade and may explain the presence of overt clinical cardiovascular disease in as many as.

SUMM . . . such as hypertension, dyslipidemia and cigarette smoking. The inventor of the present invention has popularized the term "dead zone of diabetes" to describe this phenomenon of increased cardiovascular risk even after allowing for the co-existence of other risk factors in diabetes. This "dead zone" is secondary to both the atherogenicity of insulin resistance, which precedes the onset of diabetes by at least 8 years, and the atherogenicity of undiagnosed and uncontrolled hyperglycemia, which is present for 9-12 years before diabetes is first diagnosed. Treatment of diabetes, and its related chronic symptoms and risk factors, are best treated at this early stage.

SUMM If the medical community is to have any success in attenuating the cardiovascular ravages of diabetes, it must stress interventions that reduce insulin resistance, an integral part of type II diabetes, and aggressively control blood glucose, through earlier diagnosis and improved management of diabetes. That is precisely why exercise and dietary modification will always be the mainstay of diabetic management, because both will improve insulin sensitivity and glucose control. Until recently the only available pharmacologic (sulfonylureas and insulin) interventions in this country for diabetes, poorly controlled with exercise and diet, did not address insulin resistance and were inappropriate for use in early type II diabetes. Not surprisingly, their use has failed to reduce the excessive cardiovascular morbidity of diabetes, and, indeed, may even be associated with increased risk of cardiovascular disease.

SUMM . . . to reduce insulin resistance, i.e. insulin sensitizers or enhancers, which hopefully may impact more favorably on the cardiovascular complications of diabetes. Unfortunately, these drugs require a prescription and their use in diabetes is markedly delayed, which will likely blunt their efficacy in reducing cardiovascular risk. Indeed, troglitazone was initially indicated in type II diabetes only in combination with insulin, precluding its use in early diabetes.

SUMM . . . developing in these high risk patients. There is also a need to provide an effective supplement for the treatment of diabetes and its symptoms prior to the onset of full-blown diabetes.

The present invention focuses upon a new and unique dietary supplement specifically formulated for people with diabetes and prediabetes (IGT). This formulation is based upon well-designed, randomized, placebo-controlled double-blind human studies, using specific minerals and trace minerals, antioxidant vitamins. . . improve blood glucose control, insulin sensitivity, lipid abnormalities, blood pressure, and reduce the risk of heart disease in people with diabetes.

SUMM . . . a source of chromium, an effective amount of a source of vanadium, an effective amount of a source of magnesium, vitamin

E and aspirin, and an effective amount of folic acid and alpha-lipoic acid.

SUMM . . . preferred supplement includes an effective amount of chromium polynicotinate and chromium picolinate as the chromium source, an effective amount of vanadyl sulfate as the vanadium source, an effective amount of magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex as the magnesium source, an effective amount of free 2R, 4'R, 8'R-alpha tocopherol as the natural vitamin E source, an effective amount of standardized willow bark as the source of aspirin, an effective amount of folic acid and alpha-lipoic acid, as well as sufficient amounts of vitamin and mineral supplements.

SUMM . . . about 200 mcg and about 1500 mcg chromium picolinate and/or chromium polynicotinate, between about 10 mg and about 100 mg vanadyl sulfate, and between about 300 mg and about

400 mg magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex, between about. . . about 30 days. The most preferred daily nutritional supplement contains about 1000 mcg chromium polynicotinate and/or picolinate, about 100 mg vanadyl sulfate, about 384 mg magnesium chloride, citrate, fumarate, malate, glutorate and succinate complex, about 400 I.U. free 2R, 4'R, 8'R-alpha tocopherol,. . . daily administration of the nutritional supplement. The daily doses of the anchor or key components listed above, in combination with vitamin and mineral supplements, can be used in patients to prevent the development of full blown diabetes or, where the person has diabetes, to reduce the amount of insulin required to control blood glucose levels. . . provides a dietary supplement that enhances glucose metabolism, while treating many of the secondary or risk factors that often accompany diabetes or IGT. While the supplement may be used by individuals with no apparent symptoms of diabetes, the supplement is ideal for use by individuals with IGT and diabetes to prevent, reduce or eliminate the necessity of using insulin or other anti-diabetic medications. However, the supplement contains ingredients Nutritional supplements according to the present invention are not intended to supplant other forms of diabetes and IGT treatment, such as the appropriate diet and exercise, nor does necessarily it eliminate the need for insulin. Rather,. . . . . . has been discovered that a dietary supplement containing effective amounts of metabolically available forms of vanadium, chromium, magnesium, and natural vitamin E in combination with naturally available sources of aspirin, alpha lipoic acid, and folic acid will improve the metabolism of glucose and arrest or treat many of the cardiovascular complications or risk factors associated with diabetes or prediabetes. These components perform different functions which, when administered in appropriate dosages and forms, enhance the metabolism of glucose. . . itself, while at the same time prevent or reduce the likelihood of a cardiovascular event due to complications associated with diabetes. The importance of each of these key or "anchor" components is set forth below: and building muscle mass, are scientifically unfounded, especially in its use for non diabetic individuals. Indeed, chromium supplementation, even in diabetes, is unsettled with the American Diabetes Association's Position Statement declaring, "The only known circumstance in which chromium replacement has any beneficial effect on glycemic control is. . . for chromium supplementation in those individuals who are obviously chromium deficient, the actual prevalence of chromium deficiency in people with diabetes has never been, nor could it be, established. Nonetheless, chromium deficiency is common in diabetic patients, who have lower plasma. Vanadyl Sulfate (preferred dosage range 10.00-100.00 mg.; most preferred embodiment is 100.00 mg) . . human tissue, has a well documented insulin enhancing effect in laboratory animals. After extensive studies using vanadate in diabetic rats, vanadyl sulfate 100 mg daily was found to significantly improve both hepatic and peripheral insulin sensitivity in patients with type II diabetes. Vanadyl sulfate was the preparation of vanadium chosen because it was not associated with any apparent toxicity during treatment periods of In a recently published study of moderately obese, insulin resistant type II diabetic patients, treatment with oral vanadyl

sulfate 100 mg daily for three weeks resulted in a significant drop in fasting blood glucose levels and a highly significant.

SUMM

DETD

DETD

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DETD

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DETD

DETD

cholesterol and a decline, though not statistically significant, in serum triglycerides. Using the hyperinsulinemic-euglycemic clamp, it was shown that vanadyl sulfate dramatically enhanced insulin mediated glucose disposal with an 82% increase in glucose infusion rate. There was also significant reduction in hepatic glucose production, likely secondary to a potentiation of insulin's inhibitory effect on lipolysis by vanadyl sulfate. As in the previous studies, vanadyl sulfate was well tolerated.

- DETD Magnesium, rather, magnesium deficiency, has long been known to be associated with diabetes, both type I and type II. Unlike some of the uncertainties regarding the incidence of chromium deficiency in diabetes, much more is known about the epidemiology and diagnosis of magnesium deficiency in diabetes, though discord regarding the actual prevalence of magnesium deficiency abounds. Indeed, magnesium deficiency may be the most underappreciated and underdiagnosed. . .
- DETD . . . been linked to the Reaven-Modan syndrome and underlies the well-known association of magnesium deficiency to essential hypertension, insulin resistance, hyperinsulinemia, diabetes, congestive heart failure and ischemic heart disease. Also, magnesium deficiency has been associated with an increase in platelet reactivity, a condition known to exist in patients with diabetes, and may help explain the accelerated atherosclerosis and increased rate of acute thrombotic events that so tragically define diabetes. Finally, hypomagnesemia has been implicated in the retinopathic microvascular complication of diabetes, with lower levels of magnesium predicting a greater risk of severe diabetic retinopathy.
- While it is universally accepted that magnesium deficiency is common in both type I and type II diabetes, it is unclear as to the precise incidence of this condition in diabetes. The diabetic patient is certainly at risk for developing magnesium depletion via inadequate dietary intake and gastrointestinal and renal losses, . . . very specific, assessment of magnesium depletion in the body. Even with this exceedingly insensitive measure for magnesium deficiency, patients with diabetes have a 25% to 38% prevalence of hypomagnesemia. Using much more sensitive research-oriented tests (nuclear magnetic resonance spectroscopy and magnesium-selective. . .
- DETD Still, the American **Diabetes** Association's position on screening, diagnosing and intervening for magnesium deficiency in patients with **diabetes** remains skeptical, as in the case of chromium deficiency. The inventor of the present invention believes this to be the. . .
- DETD . . . Magnesium, as used in the present invention, is thus expected to improve glucose metabolism and to arrest or reduce any diabetes associated secondary risk factors.
- DETD Vitamin E Natural (free 2R, 4'R, 8'R-alpha tocopherol)(preferred range 400.00-800.00 I.U.; most preferred dosage 400 I.U.)
- DETD Vitamin E is the most widely studied of the antioxidant vitamins. The interest in vitamin E as an antioxidant is based on the many demonstrations in humans that giving vitamin E as a supplement decreases the oxidation of low density lipoprotein (LDL) ex vivo, an event critical in the atherogenic. . .
- Vitamin E supplementation has been shown to significantly reduce experimentally induced atherosclerosis in primates and more recent epidemiological and interventional human studies appear to support this observation. This assumes greater importance in those with diabetes, in view of the fact that as many as 60% of newly diagnosed diabetic patients already have clinically obvious cardiovascular. . .
- DETD . . . disease was observed in a four year, prospective, observational

study in healthy middle-aged men who had higher intakes of dietary vitamin E as compared to those consuming small amounts.

DETD at baseline were found to have a highly significant reduced risk of coronary artery disease if they had been on vitamin E supplements for at least two years during the eight year study. In a more recent and similar seven year prospective study of postmenopausal women without cardiovascular disease, dietary vitamin E consumption, but not vitamin A or C, was inversely associated with the risk of death from coronary artery disease.

DETD Perhaps the most powerful argument for vitamin E supplementation, at least, in those patients with already proven coronary artery disease, is the recently published Cambridge Heart Antioxidant. . . The CHAOS was a nearly three year prospective, secondary interventional trial of 2002 men and women, 10% of whom had diabetes, using natural vitamin E (free 2R, 4'R, 8'R-alpha tocopherol), 400 or 800 I.U. daily, in a randomized, placebo-controlled, double-blinded design. Either dose of vitamin E was associated with a dramatic and significant 77% risk reduction of non-fatal myocardial infarct. The benefit of treatment with vitamin E was apparent after 200 days, and the patients with diabetes also enjoyed the marked reduction in the risk of non-fatal heart disease.

DETD Another unrelated benefit of vitamin E supplementation is the favorable effect it has on insulin sensitivity, glucose metabolism and lipid levels in both healthy subjects and patients with type II diabetes. Conversely, in a prospective study of almost one thousand non diabetic, middle-aged men, low concentration of plasma vitamin E at baseline was found to be an independent and powerful predictor for the development of type II diabetes during the four year study. Remarkably, a low level of vitamin E was associated with a greater than five-fold risk of developing diabetes in the ensuing four years!

DETD Vitamin E was well tolerated in the studies where it was given as a supplement, and in the CHAOS study there. . . effects. Because of the unusually high incidence of clinical heart disease in newly diagnosed diabetic patients, and the favorable effect vitamin E has on the metabolic abnormalities of type II diabetes, the present invention will contain preferably 400-800 I.U.; and most preferably natural vitamin E (free 2R, 4'R, 8'R-alpha tocopherol) 400 I.U.

DETD . . costs alone would be reduced by \$3 billion per year in this country if the 15 million adults, many with diabetes, who qualify for hypolipidemic medication per NCEP guidelines were to first be given aspirin prophylaxis.

DETD . . enzyme necessary for the synthesis of thromboxane, a potent stimulator of platelet aggregation, a condition known to be increased in diabetes and to be causative in the atherosclerotic process. In patients with diabetes, aspirin has been shown to correct this abnormal increase in platelet activity.

DETD The cardiovascular protective effect of aspirin in men and women with diabetes was demonstrated in the Early Treatment Diabetic Retinopathy Study. Both type I and II patients were randomized to double-blinded placebo.

DETD . . . of alpha-lipoic acid to diabetic patients with neuropathy significantly reduces symptoms. Diabetic neuropathy has been an unusually refractive complication of diabetes.

DETD These anchor compounds are most preferably combined with other vitamin and mineral supplements. These additional ingredients are preferably included with the anchor compounds, and should be taken simultaneously.

DETD . . . that sufficient amounts of the most important minerals and vitamins are available, it is preferred that the supplement also include

```
vitamin A (or beta carotene), vitamin C, calcium,
       copper, selenium, and zinc.
DETD
       One example of the preferred embodiment, the "Pro Health Pak," is
       distributed by Diabetes Pro Health of Pittsburgh, Pa. Pro
       Health Pak consists of two major "components." The first, the so-called
       backbone of the supplement,.
DETD
3 tablets
      Containing Chromium Polynicotinate and Picolinate, Vanadyl
        Sulfate, Vitamin E Natural, Standardized Willow Bark
       (aspirin),
      Folic Acid, Alpha-Lipoic Acid and
      a Multivitamin/Mineral Formula
1 tablet
      Containing Magnesium Complex consisting of.
DETD
Chromium Polynicotinate and Picolinate
                        200-1500 mcg.
  Vanadyl Sulfate Hydrate
                        10-100
                                 mg.
  Vitamin E Natural (free 2R, 4'R
                        400-800 I.U.
8'R-alpha tocopherol)
Standardized Willow Bark
                        160-320 mg.
(aspirin 20-40 mg.)
Magnesium Chloride, Citrate, Fumarate,
                        300-400
"common" Malate, Glutorate and
Succinate Complex
Folic Acid (Folate)
                        400-600
                                 mcg
Alpha-Lipoic Acid
                        0-600
  Vitamin A or Beta Carotene
                       5000
                                 I.U. or
                       25,000
                                 I.U.
                          60
  Vitamin C
                                   mg.
Thiamine
                       3.00
                                 mq.
Riboflavin
                       3.60
                                 mg.
Niacinamide
                       20.10
                                 mg.
                         23.10
  Vitamin B-6
                                   mg
                          48.00
  Vitamin B-12
                                   mcg.
Biotin
                       300
                                 mcg.
Pantothenic Acid
                       10.00
                                 mg.
Calcium
                       150
                                 mg.
Phosphorus
                       115
                                 mg.
                       150
Iodine
                                 mcq.
Zinc
                       15.00
                                 mq.
Selenium
                       60
                                 mcg.
                       2.00
Copper
                                 mg.
Manganese.
DETD
               containing a 30 day supply. The daily supplement is provided as
       an individual packet in which 4 tablets are enclosed. Diabetes
       Pro Health provides to the patient with diabetes or pre-
       diabetes a readily available and affordable and medically proven
       addition to their armamentarium for diabetes management,
       something which has been sorely lacking. Pro Health Pak will be
       recommended for use in patients with diabetes or pre-
       diabetes only as part of a complete diabetes treatment
       or prevention program, and will require regular blood glucose monitoring
       when used in the diabetic patient.
```

The daily dietary supplement of claim 1, further comprising: (e) an

CLM

What is claimed is:

effective amount of a source of vitamin E natural.

- 10. A daily dietary supplement according to claim 9, wherein said source of vanadium is vanadyl sulfate.
- 14. A daily dietary supplement according to claim 2, wherein said effective amount of **vitamin** E natural is in the range of about 400 IU up to about 600 IU.
- . effective amount of a source of vanadium; and (d) an effective amount of one or more of a source of **vitamin** E natural or a source of folic acid.
- 22. A daily dietary supplement according to claim 15, wherein said source of vanadium is **vanadyl sulfate**.
- 25. A daily dietary supplement according to claim 15, wherein said source of **vitamin** E natural is included and said effective amount of **vitamin** E natural is in the range of about 400 IU up to about 600 IU.
- 38. A method according to claim 28, wherein said source of vanadium is vanadyl sulfate.
- 41. A method according to claim 28, wherein said patient has diabetes or a pre-diabetic condition.
- . one or more of an effective amount of a source of folic acid, an effective amount of a source of **vitamin** E or an effective amount of a source of lipoic acid.
- . one or more of an effective amount of a source of folic acid, an effective amount of a source of **vitamin** E or an effective amount of a source of lipoic acid.
- 53. A method according to claim 44, wherein said source of vanadium is vanadyl sulfate.
- 57. A method according to claim 45, wherein said effective amount of **vitamin** E natural is in the range of about 400 IU up to about 600 IU.
- 58. A method according to claim 44, wherein said patient has diabetes or a pre-diabetic condition.
- . 650 up to about 1500 .mu.g of chromium polynicotinate, in the range of about 10 up to about 100 mg vanadyl sulfate hydrate, in the range of about 400 up to about 800 I.U. vitamin E natural (free 2R, 4'R, 8'R-alpha tocopherol), in the range of about 300 up to about 400 mg magnesium chloride, . . .
- AN 1999:120934 USPATFULL
- TI Dietary supplement and method of treatment for diabetic control|
- IN Fine, Stuart A., Northbrook, IL, United States
- PA Akesis Pharmaceuticals, Inc., La Jolla, CA, United States (U.S. corporation)
- PI US 5962030 19991005
- AI US 1997-964814
- 19971105 (8)
- PRAI US 1997-39958P
- 19970307 (60)
- DT Utility
- FS Granted|
- EXNAM Primary Examiner: Jarvis, William R. A. |-
- LREP Gray Cary Ware & Freidenrich, Reiter, Stephen E. |

CLMN Number of Claims: 60|
ECL Exemplary Claim: 1|
DRWN No Drawings

LN.CNT 1156|

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
Utility
DT
       APPLICATION
FS
LN.CNT 19583
       INCLM: 435/069.100
INCL
       INCLS: 435/325.000; 435/320.100; 536/023.200
              435/069.100
NCL
              435/325.000; 435/320.100; 536/023.200
       NCLS:
IC
       [7]
       ICM: C12P021-02
       ICS: C12N005-06; C12N015-74; C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 106 OF 113 USPATFULL
L1
       2002:66896 USPATFULL
AN
       ABC transport polynucleotides, polypeptides, and antibodies
TI.
       Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
       Moore, Paul A., Germantown, MD, UNITED STATES
                           Α1
                                20020328
PΙ
       US 2002037549
                                20010124 (9)
       US 2001-767870
                          A1
ΑI
       Continuation-in-part of Ser. No. WO 2000-US19736, filed on 20 Jul 2000,
RLI
       UNKNOWN
                            19990723 (60)
       US 1999-145215P
PRAI
       US 1999-149445P
                            19990818 (60)
       US 1999-164730P
                            19991112 (60)
DT
       Utility
FS
       APPLICATION
LN.CNT 12219
INCL
       INCLM: 435/069.100
       INCLS: 435/006.000; 435/007.100; 435/183.000; 435/325.000; 536/023.100
NCL
       NCLM:
              435/069.100
              435/006.000; 435/007.100; 435/183.000; 435/325.000; 536/023.100
       NCLS:
       [7]
IC
       ICM: C12Q001-68
       ICS: G01N033-53; C07H021-04; C12N009-00; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 107 OF 113 USPATFULL
L1 '
       2002:66870 USPATFULL
AN
       IL-6-like polynucleotides, polypeptides, and antibodies
TΙ
       Ruben, Steven M., Olney, MD, UNITED STATES
IN
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       US 2002037523
                                20020328
ΡI
                           A1
                                20010607 (9)
                           A1
ΑI
       US 2001-875016
       Continuation-in-part of Ser. No. WO 2000-US33134, filed on 7 Dec 2000,
RLI
       UNKNOWN
       US 1999-169838P
                            19991209 (60)
PRAI
DT
       Utility
FS
       APPLICATION
LN.CNT 11587
INCL
       INCLM: 435/006.000
       INCLS: 536/023.500; 435/007.100; 435/069.520; 435/320.100; 435/325.000;
              530/351.000; 424/085.200
              435/006.000
NCL
       NCLM:
              536/023.500; 435/007.100; 435/069.520; 435/320.100; 435/325.000;
       NCLS:
               530/351.000; 424/085.200
IC
       ICM: C120001-68
       ICS: G01N033-53; C07H021-04; C12P021-04; A61K038-20; C12N005-06;
       C07K014-54
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

```
ANSWER 108 OF 113 USPATFULL
T.1
       2002:22131 USPATFULL
ΑN
       18 Human secreted proteins
TI
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
ΙN
       Young, Paul E., Gaithersburg, MD, UNITED STATES
       Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
       Soppet, Daniel R., Centreville, VA, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
                          A1
                               20020131
PΙ
       US 2002012966
       US 2001-768826
ΑI
                          A1
                               20010125 (9)
       Continuation-in-part of Ser. No. WO 2000-US22350, filed on 15 Aug 2000,
RLI
       UNKNOWN
       US 1999-148759P
                           19990816 (60)
PRAI
       Utility
DT
FS
       APPLICATION .
LN.CNT 18157
INCL
       INCLM: 435/069.100
       INCLS: 435/325.000; 435/183.000; 530/350.000; 536/023.100
NCL
             435/069.100
              435/325.000; 435/183.000; 530/350.000; 536/023.100
IC
       [7]
       ICM: C12P021-02
       ICS: C07H021-04; C12N009-00; C12N005-08
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 109 OF 113 USPATFULL
L1
       2002:12261 USPATFULL
ΑN
ΤI
       Uteroglobin-like polynucleotides, polypeptides, and antibodies
       Ni, Jian, Germantown, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002006640
                          A1
                               20020117
ΑI
       US 2001-846258
                          A1
                               20010502 (9)
       Continuation-in-part of Ser. No. WO 2000-US30326, filed on 3 Nov 2000,
RLI
       UNKNOWN
       US 1999-163395P
                           19991104 (60)
PRAI
DT
       Utility.
FS
       APPLICATION
LN.CNT 12076
INCL
       INCLM: 435/069.100
       INCLS: 435/325.000; 435/006.000; 435/007.100; 514/044.000; 530/350.000;
              536/023.500
NCL
       NCLM:
              435/069.100
              435/325.000; 435/006.000; 435/007.100; 514/044.000; 530/350.000;
       NCLS:
              536/023.500
IC
       [7]
       ICM: C12P.021-02
       ICS: C12N005-06; A61K048-00; C07K014-72; C12Q001-68; G01N033-53;
       C07H021-04
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 110 OF 113 USPATFULL
L1
AN
       2002:8489 USPATFULL
       Retinoid receptor interacting polynucleotides, polypeptides, and
ΤI
       antibodies
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002004489
                          A1
                               20020110
ΑI
       US 2001-788600
                          Α1
                                20010221 (9)
       Continuation-in-part of Ser. No. WO 2000-US22351, filed on 15 Aug 2000,
RLI
       UNKNOWN
PRAI
       US 1999-148757P
                           19990816 (60)
       US 2000-189026P
                           20000314 (60)
```

```
DT
       Utility
       APPLICATION
FS 1
LN.CNT 11257
       INCLM: 514/044.000
INCL
       INCLS: 536/023.500; 530/350.000; 435/069.100; 435/325.000; 530/388.220
NCL
       NCLM:
              514/044.000
              536/023.500; 530/350.000; 435/069.100; 435/325.000; 530/388.220
       NCLS:
IC ·
       [7]
       ICM: A61K048-00
       ICS: C07H021-04; C12P021-02; C12N005-06; C07K014-705; C07K016-28
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
T.1
     ANSWER 111 OF 113 USPATFULL
       2001:152504 USPATFULL
AN
       Pharmaceutical compositions of vanadium biguanide complexes and their
ΤI
       Orvig, Chris, Vancover, Canada
IN
       McNeill, John H., Vancouver, Canada
       The University of British Columbia, Vancouver, Canada (non-U.S.
PA
       corporation)
       US 6287586
                                20010911
PΙ
       US 1999-396982
                                19990915 (9)
ΑI
       US 1998-101074P
                           19980918 (60)
PRAI
       Utility
DT
       GRANTED
FS
LN.CNT 798
       INCLM: 424/423.000
INCL
       INCLS: 514/184.000; 514/866.000
NCL
              424/423.000
       NCLM:
              514/184.000; 514/866.000
       NCLS:
IC
       [7]
       ICM: A61K009-10
       ICS: A61K031-28
       514/184; 514/866; 424/464; 424/451; 424/489; 424/499; 424/423; 424/436;
EXF
       424/45
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 112 OF 113 USPATFULL
L1
AN
       1999:37095 USPATFULL
ΤI
       Composition and method for treating diabetes
       Gutierrez, Enrique G., 5212 Wade Dr., Metairie, LA, United States 70003
IN
       Leboeuf, Reynold, Houma, LA, United States
       Gutierrez, Enrique G., Metaire, LA, United States (U.S. individual)
PA
       US 5885980
                               19990323
PΙ
                                19960625 (8)
ΑI
       US 1996-669939
DT
       Utility
FS
       Granted
LN.CNT 461
INCL
       INCLM: 514/186.000
       INCLS: 514/593.000
              514/186.000
NCL
       NCLM:
              514/593.000
       NCLS:
       [6]
IC
       ICM: A61K031-555
       ICS: A61K031-175
       514/186; 514/593
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L1
     ANSWER 113 OF 113 USPATFULL
AN
       1998:153865 USPATFULL
       Composition and method for reducing blood sugar levels in diabetic
ΤI
```

humans

```
Al-Dahir, Holly Christine, 4521 Conlin St., Metairie, LA, United States
ΙN
       70006
                               19981208
       US 5846544
ΡI
       US 1997-891590
                               19970711 (8)
ΑI
DT
       Utility
       Granted
FS
LN.CNT 245
       INCLM: 424/195.100
INCL
       INCLS: 514/783.000; 514/866.000; 514/884.000
       NCLM: 424/732.000
NCL
       NCLS: 514/783.000; 514/866.000; 514/884.000
       [6]
IC
       ICM: A61K035-78
       424/195.1; 514/783; 514/866; 514/884
EXF
=> d 11 112-113 kwic, bib
     ANSWER 112 OF 113 USPATFULL
T.1
       Composition and method for treating diabetes
TΙ
       A method of treating diabetes in a patient in need thereof,
AB
       comprising administering to said patient a therapeutically effective
       amount of a pharmaceutically acceptable VO.sup.+2.
       The present invention is directed to compositions and methods of using
SUMM
       the same for the treatment of diabetes. The composition
       includes a combination of the oral hypoglycemic agent micronized
       glyburide and a trace rare metal supplement, such as.
       Vanadyl sulfate (VOSO.sub.4), which is readily
SUMM
       available over the counter in the United States at local health food
       stores, is marketed as a nutritional supplement. Although it is used for
       other purposes as well, vanadyl sulfate has been
       taken to improve glycemic control. Vanadyl sulfate
       generates the vanadyl radical (VO.sup.-3) which has been shown to
       reverse diabetes in pancreatectomized rats. The radical
       (VO.sub.3.sup.-) is the predominate radical form in extracellular fluid.
       It is reduced intracellularly into the.
            . been numerous publications in the medical scientific literature
SUMM
       demonstrating that vanadyl radical generating compounds have exceptional
       antidiabetic effects in animals. Vanadyl sulfate
       orally administered to animals has been shown to produce normoglicemia
       which can persist even after discontinuation of the therapy.
            . in humans have been unsuccessful. Recent published human trials
SUMM
       show only a mild improvement in glycemic control with administration of
       vanadyl sulfate.
       A third factor involves toxicity. Compounds which tend to have greater
SUMM
       cellular penetration typically exhibit greater toxicity levels. In
       particular, vanadyl sulfate (VOSO.sub.4) is 1/10 as
       toxic than other vanadyl radical generating compounds. However, this
       compound has a lower antidiabetic potency than.
SUMM
       Oral hypoglycemic agents such as tolazamide, tolbutamide,
       chlorpropamide, micronized and non-micronized glyburide,
       glimepiride, glypizide, metformin, and phenformin have been available as
       oral treatments for diabetes, typically non-insulin dependent
       (Type II) diabetes. Oral hypoglycemic agents in general are
       disadvantageous because the extent , predictability and duration of the
       antidiabetic effect is unpredictable.
SUMM
       It would therefore be a significant advance in the art of treating
       diabetes to provide a composition which can effectively treat
       both Type I and Type II diabetes and which can provide
       effective glycemic control for all, including patients who cannot
       effectively utilize or are resistant to insulin.
SUMM
       The present invention is directed to a composition and method for the
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treatment of Type I and Type II diabetes and complications arising therefrom comprising a therapeutically effective amount of each of:

- SUMM The present invention is also directed to a method of treating diabetes comprising administering to a warm blooded animal, including humans, a therapeutically effective amount of the composition of the present invention.
- DRWD . . . graph showing glucose levels for the treatment of a Type II adult onset diabetic patient using Glynase (micronized glyburide) alone, vanadyl sulfate alone and the composition of the present invention;
- DETD The present invention is directed to a composition and method of treating warm blooded animals, including humans suffering from diabetes with a pharmaceutical composition comprising a VO.sup.+2 generating compound together with micronized glyburide as the active agents. The active agents. . .
- DETD . . . administered to a warm blooded animal). Examples of vanadyl compounds include sodium orthovanadate, sodium metavanadate, bis oxovanadium, sodium metavanadate (NaVO.sub.3), vanadyl sulfate (VOSO.sub.4), sodium orthovanadate (Na.sub.3 VO.sub.4), ammonium metavanadate (NH.sub.4 VO.sub.3.sup.-), aluminum orthophosphate vanadia (V.sub.2 O.sub.5 -AlPO.sub.4), diperoxovanadate, bis(maltolato)oxovanadium(IV)(BMOV), VOCl.sub.3, VOCl.sub.21 VCl.sub.3,.
- DETD . . . of VO.sup.+2 generating compounds on the basis of the weight of the element vanadium. The preferred VO.sup.+2 generating compound is vanadyl sulfate in part because it is considered least toxic.
- DETD . . . the compound necessary to obtain the desired amount of the VO.sup.+2 radical can be readily calculated. By way of example, vanadyl sulfate (VOSO.sub.4) can generally be administered in an amount of from about 10 to 120 mg/day, preferably from about 30 to 90 mg/day, most preferably from about 60 to 90 mg/day. Vanadyl sulfate is commercially available as a nutritional supplement from several sources including GNC health food stores. The required dosage amount may. . .
- DETD For example, a typical daily dosage of **vanadyl sulfate**and micronized glyburide based on the extent of loss of glycemic control
  or for insulin resistance for a typical patient. . .
- DETD . . . from about 4 to 12 weeks. During the period of administration the total amount of the VO.sup.+2 generating compound (e.g. vanadyl sulfate) administered is generally from about 1000 to 3000 mg. Shorter or longer durations of treatment can be employed depending on . .
- DETD In a preferred form of the invention for the treatment of diabetes a dosage of 60-90 mg of vanadyl sulfate and 6-12mg of micronized glyburide are administered once daily, preferably in the morning for at least 8 weeks and up. . . at the normal or near normal ranges. Thereafter, the dosage regimen is reduced to 6 mg of glyburide/60 mg of vanadyl sulfate administration. Glycemic control is achieved independently of insulin production.
- The active components (e.g. vanadyl sulfate and micronized glyburide) are commercially available and can be utilized as such in the present invention. However, if fixed combination. . . appropriate dosage form according to known techniques in the art. Ideally a tablet containing 3 mg glyburide and 30 mg vanadyl sulfate would be most practical for this purpose.
- DETD A 57 year old smoker was diagnosed with **diabetes** in 1992. He had concurrent severe coronary artery disease which required angioplasty several years prior to 1992. As shown in. . . a low of 130 mg/dl to a high of above 350 mg/dl. Glynase administration was stopped followed by

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administration of vanadyl sulfate at a daily dosage of 60 mg. As shown in FIG. 1, glucose levels were slightly improved but nonetheless glucose. . .
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- DETD Thereafter, the subject received 60 mg of vanadyl sulfate and 6 mg of Glynase per day for a period of approximately one month. There was an immediate and significant.
- DETD Thereafter for a period of approximately one week, the amount of vanadyl sulfate was increased to 70 mg per day and there was a further drop of glucose level to approximately 110 mg/dl.... of from about 90 to 110 mg/dl. Glynase therapy was discontinued and the subject was placed on 15 mg of vanadyl sulfate per day with glucose levels remaining below about 110 mg/dl. Thereafter all medication was discontinued and the patient maintained normal.
- DETD As shown with the subject discussed in Example 1, the combination of vanadyl sulfate and Glynase resulted in a significant lowering of glucose levels and maintenance of glucose levels within a narrow, normal range.. . .
- DETD A 59 year old black female had a seven year history of **diabetes** mellitus. When the subject was first tested as shown in FIG. 2, she was taking glucotrol (20 mg) which is. . .
- DETD Thereafter, the patient was administered 25 units of insulin per day plus 60 mg of vanadyl sulfate and 6 mg of Glynase over the course of approximately 6 months. Glucose levels dropped from a high of about. . .
- DETD Thereafter, insulin therapy was discontinued but the subject continued to receive 60 mg of vanadyl sulfate with 9 mg of generic Glynase per day. As a result, the subject's glucose levels remained at the lowest levels. . .
- DETD A 14 year old white female was diagnosed with Type I juvenile insulin dependent diabetes mellitus at the age of 11. From the age of 11 to 13 she exhibited poorly controlled glucose levels with. . .
- DETD . . . of insulin in the evening as per established therapy.

  Thereafter, insulin administration was continued and the combination of 60 mg vanadyl sulfate and 6 mg of Glynase was added to the insulin therapy administered daily over the course of approximately 6 weeks. . .
- DETD Thereafter, vanadyl sulfate/Glynase therapy was continued and insulin therapy was reduced, first to 12 units per day, then to 10 units per day. . .
- DETD A 77 year old white male was diagnosed with insulin dependent diabetes mellitus. He was considered to be a brittle diabetic. He had extreme difficulty with frequent hypoglycemic events where blood sugar. . .
- DETD . . . 500 mg of glucophage, a known oral anti-diabetic drug as well as 6 mg of Glynase and 60 mg of **vanadyl sulfate** along with insulin with 30 units in the morning and 15 units in the evening in an effort to stabilize. . .
- DETD A 42 year old black female developed type I juvenile insulin dependent diabetes at age 8. Over the years she developed progressively greater insulin resistance (acanthosis nigricans).
- DETD Thereafter the subject received both **vanadyl sulfate**(80 mg) and Glynase (12 mg) which reduced the daily insulin requirement to only 200 units from 1,200 and furthermore. . .
- CLM What is claimed is:

  1. A pharmaceutical composition for use in the treatment of diabetes, said composition comprising a therapeutically effective amount of: (a) VO.sup.+2 generating compound selected from the group consisting of sodium orthovanadate, sodium metavanadate, bis oxovanadium, sodium metavanadate (NaVO.sub.3), vanadyl sulfate (VOSO.sub.4), sodium orthovanadate (Na.sub.3 VO.sub.4), ammonium metavanadate (NH.sub.4 VO.sub.3), aluminum orthophosphate vanadia (V.sub.2 O.sub.5 AIPO.sub.4), diperoxovanadate, bis (maltolato)

being 6'4" in height, having a history of **diabetes** from the distaff side, diagnosed with Type II (insulin resistance) for four years, was being maintained on an insulin dosage. . .

DETD A fifty-five year old Caucasian male weighing 335 pounds and standing 5'6" tall had Type II non-insulin dependent **diabetes** mellitus for four years, being maintained on a sulfonylulurea hypoglycemic agent, specifically **chlorpropamide**, as well as being maintained on a blood pressure medication and a weight controlled medication, and not on a diabetic. . .

DETD It is noted that, beginning one month before initial dosage of the herbs, subject took vanadyl sulfate (5,000 mcg) chromium picolinate (250 mcg), and a multi-vitamin capsule once daily with a meal, with no effect on blood sugar level. Vanadyl sulfate and chromium picolinate are know hyproglycemic agents. When subject's blood sugar level was reduced to approximately 200 mg/dl, subject began. . .

DETD A male Caucasian, 17 years of age, 5'2" in height, 116 pounds having Type I diabetes mellitus diagnosed in November, 1995, one year before herbal treatment commenced, was very active and strenuously exercised daily, was on. . .

DETD Subject is on vitamin and mineral supplements, including vanadyl sulfate and chromium picolinate and gymnema sylvestre, which are known hypoglycemic agents.

DETD Based upon the test results, the treatment for adult onset (Type II diabetes) requires ingestion of bilberry fruit (approximately 375 milligrams of the milled herb) and valerian root approximately 400 to (450 to. . .

DETD . . . reducers such as penicillin and its derivatives such as, amoxycillin, as well as mineral hypoglycemic agents as chromium picolinate and vanadyl sulfate, (iv) insulin dependent diabetes mellitus subjects will experience hyperglycemia especially in the early stages of treatment if the bilberry and valerian are discontinued or. . .

AN 1998:153865 USPATFULL

TI Composition and method for reducing blood sugar levels in diabetic humans

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PI US 5846544 19981208

AI US 1997-891590 19970711 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Prats, Francisco C.

LREP Carbo, Michael D. CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 245